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BRITISH MEDICAL JOURNAL

LONDON SATURDAY JUNE 18 1955

EFFECTS OF DIETARY PROTEIN, LIPOTROPIC FACTORS, AND RE-ALIMENTATION ON TOTAL HEPATIC LIPIDS AND THEIR DISTRIBUTION

BY

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[WITH SPECIAL PLATE]

Interest in the distribution of fat within the liver lobule has been stimulated by the observation that in the widespread disease kwashiorkor the stainable fat is found predominantly in the periportal regions. This subject has recently been reviewed by Brock (1954). It is, of course, a long step from the distribution of fat in the liver of the human infant to that seen in the rat, even when an attempt is made to utilize diets similar to those that produce the characteristic lesions in the human liver. The initial distribution of fat under standardized experimental conditions may not be the same as that which is seen at a later stage. Our lack of knowledge of the anatomy and physiology of the liver lobule prevents us from explaining the mechanisms which determine the localization of fat even when this is sharply defined and consistently reproducible. However, experimental work is steadily revealing new facts that are contributing to the solution of these problems.

In choline deficiency in the rat the first appearance of stainable fat is in the area around the central veins (Lillie, Ashburn, Sebrell, Daft, and Lowry, 1942; Glynn, Himsworth, and Lindan, 1948; Hartroft, 1950). In fasted rats given anterior pituitary extract the initial distribution of the fat is definitely periportal (Best, Hartroft, and Sellers, 1952). Some years ago Dible reported that in rats and rabbits during starvation the distribution of fat is sometimes mainly periportal (Dible, 1932; Dible and Libman, 1934). Shils and Stewart (1954a) have drawn attention to the periportal distribution of fat in the livers of rats fed corn-meal diets and remarked upon the similarity of the lesion to that described by many clinicians in children suffering from kwashiorkor. A similar distribution has been noted in rats consuming other plant materials, such as rice, cassava, and wheat flour (Shils, Friedland, and Stewart, 1954).

Several reports of fatty livers not responding to the usual supplements of choline or its precursors have appeared recently (Wang, Hegsted, Lapi, Zamcheck, and Black, 1949; Litwack, Hankes, and Elvehjem, 1952; Sauberlich, 1953; Singal, Hazan, Sydenstricker, and Littlejohn, 1953; Harper, Monson, Benton, and Elvehjem, 1953; Harper, Monson, Benton, Winje, and Elvehjem, 1954; Winje, Harper, Benton, Boldt, and Elvehjem, 1954). The basal diets fed to the rats in which this condition has been encountered have usually been low in protein. Under these conditions choline has often failed to maintain the liver fat within the normal range, although it has generally prevented any great increase in total liver lipids.

We wish to report some effects of varying the nature and amount of protein in the diet on the total lipids and distribution of stainable fat in the livers of rats and on the lipotropic effect of choline in these diets. Histological studies suggest that the abnormal lipid whose accumulation is not prevented by choline has a different distribution from that seen when the deficiency involves choline or its precursors. It was also noted, during a study of the accumulation and removal of stainable fat in periportal regions, that re-alimentation after diminished food intake due to dietary (protein) deficiency resulted in a transitory fatty liver, the demonstrable fat being exclusively periportal in distribution.

Methods

Five separate experiments will be reported involving some 300 albino (Wistar) rats. The animals were kept in individual cages with a false bottom of coarse wire screen. Fresh food and water were supplied each day; food intake was recorded daily and rats were weighed weekly. Unless otherwise stated, the animals were fed the diets *ad libitum* for three weeks and were then killed by stunning and exsanguination. Livers were removed at once and weighed. Portions were taken for histological examination, and the remainder of the tissue was analysed for total lipids (extraction with hot alcohol, rectification of the lipid residue with a mixture of petroleum ether and chloroform 3:1 v/v). The percentage composition of the basal diets fed in each experiment is shown in Table I. It should be noted that in these studies vitamin B_{12} (300 μg. per 100 g.) was added to the vitamin mixture described by Ridout, Lucas, Patterson, and Best (1954), thus providing 3 μg. per 100 g. of ration. Basal diets are identified by the numerical suffix -0 (Tables I, II, III, and IV).

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Histological Examination

The distribution of demonstrable fat in the livers was studied in frozen sections (5 μ) of formalin-fixed tissues using Wilson's trichrome–oil red 0 technique. Paraffin sections (5 μ) of Bouin-fixed tissues were stained with haematoxylin and eosin.

The sections were examined under a code number by one of us (W. S. H.). The amount of demonstrable lipid was graded from 0 to ++++ (Special Plate, Figs. 1 to 8). Although in Tables II, III, and IV the distribution of the lipid is recorded merely as periportal or centrolobular, the degree of localization varied considerably. The term "periportal" was applied not only when the fat-containing cells were restricted to regions immediately surrounding the portal vein and hepatic artery alone, but also when this distribution extended much farther towards the central vein but did not envelop it. In almost all cases, however, the lobular distribution of the lipid was remarkably clear and well defined, as shown in the figures. Often there was evidence of increased glycogen deposition, especially in the periportal regions (cf. Ramalingaswami, Sriramachari, and Patwardhan, 1954).

Dietary Conditions

In *Experiment I* the lipotropic effect of choline was compared in diets containing different amounts of protein (casein). In these diets (Ia, Ib, Ic, and Id, Table I) the total methionine was kept constant at 0.54% by adding sufficient supplementary DL-methionine. This amount of methionine is equal to that present in the last diet, which contains 18% casein. Groups of six male rats (weighing 70 to 90 g.) were fed these basal diets supplemented with choline chloride as shown in Table II.

In *Experiment II* the rats were fed an animal protein (fibrin), a vegetable protein (soya bean), and mixtures of the two (Table I). Again, in this experiment enough DL-methionine was added to all diets (except IIe) to bring the total to 0.54%. Groups of eight male rats (65 to 80 g.) were fed these basal diets supplemented with choline chloride as shown in Table II.

Experiment III permits comparison of the effect on the distribution of stainable fat in the livers of feeding a low-protein diet (3% casein) without supplementary methionine (Diet IIIa) and with supplementary methionine (Diet Ia). A similar comparison was made in high-protein diets containing less than half as much methionine (250 mg.) as does 18% casein (Diets IIIb and Id respectively). Groups of ten female rats (65 to 90 g.) were fed the basal diets IIIa-0 and IIIb-0 (Table I), alone or supplemented with choline chloride (0.5%), as shown in Table III. Four groups were fed *ad libitum*; rats of the fifth group (IIIb-0 p.f.) were fed the same average amounts of food each day as were consumed by those in Group IIIa-0.

In *Experiment IV* the effect was studied of prolonged consumption of a diet very low in vegetable protein (soya protein 2% plus peanut protein 1%). This ration (IVa-0, Table I), which contains only 32 mg. methionine per 100 g. of mixture, was variously supplemented with choline chloride (0, 0.36%, and 1%, Table III) and fed *ad libitum* for 85 days to male rats (180 to 200 g.).

Experiment V was planned to supply data on the time relationships of both the accumulation of periportal liver lipids in rats on a low-protein diet and their removal when the animals were transferred to a "curative" diet high in protein (Table I, Diets Va and Vb respectively). Forty female rats (65 to 80 g.) were fed the low-protein diet (Va-0, 3% casein), which was supplemented with methionine to make it equivalent in that respect to the "curative" diet containing 18% casein; both diets contained 0.5% choline chloride. Pairs of rats were killed after being fed the low-protein diet for 2, 4, 8, and 16 days, respectively. The remaining 32 rats were transferred to the "curative" diet (Vb containing 18% casein). Groups of eight rats were killed after consuming the "curative" diet for 3, 7, 14, and 21 days, respectively. In addition 25 similar rats were fed a commercial stock ration ("master fox chow," Toronto Elevators, Ltd.). During the first 16 days these rats were pair-fed with those given the low-protein diet. Five rats were killed at the end of this time, and the remainder were then allowed to eat the chow *ad libitum*; groups of five rats were killed after 3, 7, 14, and 21 days, respectively.

Results

Livers from many normal rats of our colony have been examined during past years. The livers were subjected to chemical analysis and sections treated with oil red 0 were scrutinized carefully. Normal values for total liver lipids by our methods of extraction and rectification range from 5 to 8%, the mean and standard error being 6.62 ± 0.09. The values for 20 male rats were 5.19 to 7.48, mean 6.31 ± 0.14; and for 38 females, 5.9 to 8.03, mean 6.79 ± 0.10. No histologically demonstrable fat could be seen in most livers (Plate, Fig. 1a). Recently, since the above experiments were completed, we have been reinvestigating the "normal" rats of our colony and have found a more frequent appearance of fat in at least some hepatic parenchymal cells. This fat often occurs only as a few to many fine droplets per cell, but occasionally some cells (2 to 12 per high-power field) are seen to be filled with fat (Plate, Fig. 1b). These latter cells appear to be distributed at random within the hepatic lobules. This increased frequency of appearance of cells containing stainable fat is being investigated further.

Experiment I

Most of the stainable fat in the livers of rats consuming the basal diets low in casein (Ia-0, Ib-0, and Ic-0) was in periportal regions, with only a trace in centrolobular areas (see Table II and Plate, Fig. 2). It should be noted that these diets contained considerable methionine. We believe that adequacy of this choline precursor in these basal diets has been important in keeping the centrolobular areas clear. Even with 0.36% of choline chloride the amount of fat in periportal regions was not significantly reduced (cf. Plate, Fig. 2b). As the amount of protein in the diet was increased, less total lipid and periportal fat was observed; only traces of periportal fat could be detected when the diet contained 18% casein (Id-0). The lipotropic effect of a given amount of choline (as estimated by chemical analysis of liver tissue) improved as the protein content of the diet increased, but even large doses of choline were unable to prevent some deposition of abnormal fat so long as the protein in the diet was low.

Experiment II

The limited effectiveness of choline chloride in maintaining normal liver lipids is seen in other diets low in protein —for example, soya protein and a mixture of soya protein with fibrin. Diet IIa-0 (9% soya protein) gave total liver lipids of 9.0% (Plate, Fig. 3); even 0.36% choline chloride failed to reduce this value significantly. As in Experiment I, the deposition of centrolobular fat was prevented by choline, but the stainable fat in periportal regions was much less affected. Fibrin at 9% (Diet IIb-0) produced lower total lipids (by chemical analysis 6.7%) and considerably less stainable fat in periportal regions than did the soya protein, but the livers were not normal. Addition of choline chloride did not appreciably alter the findings (Plate, Fig. 4). A mixture of these two proteins at a total protein level of 9% (Diet IIc-0) also permitted the deposition of considerable periportal fat that was not affected by choline, although some prevention of lipid deposition could be shown analytically. Twice as much of the same protein mixture (that is, soya protein 12% plus fibrin 6%, Diet IId-0) resulted in a more nearly normal liver: only a trace of stainable fat could be detected in periportal regions and only a faint trace in the centrolobular area. Choline reduced the total lipid, but did not alter appreciably that seen in periportal regions.

The results when rats were fed Diet IIe-0 are of particular interest (Plate, Fig. 5). This ration was the same as Diet IId-0 except that the supplementary methionine was omitted. In the absence of this choline precursor the liver became very fatty (27% total lipids), the bulk of the stainable fat appearing in centrolobular position (+++ to ++++). Since the distribution of fat was diffuse throughout the lobule the amount in periportal regions was difficult to estimate, but it was recorded as +. A small supplement of choline chloride (0.12%) reduced the total lipids to 6.5% —that is, within the normal range—but a small amount of stainable fat could still be seen around the central vein as well as in the periportal region. Had more choline been given, this centrolobular fat would probably have been eliminated.

Experiment III

The well-established fact that choline deficiency leads to an accumulation of fat in the centrolobular region was confirmed, as was the newer observation that stainable fat in the periportal region is connected with protein inadequacy. The ration containing 3% of casein without supplementary methionine (Diet IIIa-0) was not eaten well; it caused a

TABLE I.—*Percentage Composition of Basal Diets*

(All diets contained a constant portion amounting to 6.02%*)

Component	Diet I				Diet II					Diet III		Diet IV	Diet V	
	a	b	c	d	a	b	c	d	e	a	b		a	b
Casein	3	6	9	18	—	—	—	—	—	3	3	—	3	18
Fibrin	—	—	—	—	—	9	3	6	6	—	—	—	—	—
Soya protein†	—	—	—	—	9	—	6	12	12	—	10	2	—	—
Peanut meal‡	—	—	—	—	—	—	—	—	—	—	10	2	—	—
Corn (maize) oil	5	5	5	5	5	5	5	5	5	2	2	—	2	2
Beef fat	—	—	—	—	—	—	—	—	—	10	10	—	10	10
Primex§	—	—	—	—	—	—	—	—	—	—	—	20	—	—
L-Cystine	—	—	—	—	—	—	—	—	—	—	—	0·27	—	—
DL-Methionine	0·45	0·36	0·27	0	0·45	0·33	0·41	0·28	0	0	0	0	0·45	0
Choline chloride	—	—	—	—	—	—	—	—	—	—	—	—	0·50	0·50
Sucrose	To make total 100 in each case													

* The constant portion consisted of "celluflour" (a non-nutritive powdered cellulose to supply bulk, obtainable from Chicago Dietetic Supply House, Chicago, Ill.) 2%, cod-liver-oil concentrate 0.010%, (Ayerst, McKenna, and Harrison, Ltd., Montreal; contains 200,000 i.u. vitamin A and 50,000 i.u. vitamin D per gramme), α-tocopheryl acetate 0.010%, salt mixture 3%, and sucrose-vitamin mixture 1%. The last two items are described fully by Ridout *et al.* (1954). Diet IV contained extra tocopheryl acetate to give a total of 0.035%.

† "Alpha protein" (Soya Products Division, Glidden Co., Chicago, Ill.) washed with water to remove traces of sulphite.

‡ Defatted peanut meal, washed with 50% ethanol to remove free and bound choline.

§ "Primex" (hydrogenated vegetable oil), obtainable from Proctor and Gamble, Ltd.

TABLE II.—*Effect of the Nature and Amount of Dietary Protein on the Lipotropic Potency of Choline*

(Sufficient DL-methionine added to keep total constant at 0.54% in all diets except IIe-0. Male rats (65 to 90 g.) fed rations for three weeks)

Experiment and Diet No.	Choline Chloride (%)	Average Daily Food Intake (g.)	Average Change in Weight (g.)	Total Lipids (% Liver Wt.)	Lobular Distribution of Stainable Fat			
					Portal		Central	
					Range	Mode	Range	Mode
Ia–0 (6)*	0	5·6	−8	12·5	+/+++	++±	0/+	f.tr.
Ia–1 (6)	0·12	4·6	−9	16·0	+/++++	++±	0/±	f.tr.
Ia–2 (6)	0·36	4·9	−10	9·9	±/++	+	0/tr.	0
Ib–0 (6)	0	5·9	+5	9·8	±/+++	+	0	0
Ib–1 (6)	0·12	7·1	+15	11·3	±/++	+	0/±	0
Ic–0 (6)	0	9·6	+54	10·7	+/++	±+	0/±	f.tr.
Ic–1 (6)	0·12	10·5	+61	9·1	+/+++	++	0/±	0
Ic–2 (6)	0·36	10·2	+61	6·8	+/++	+	0/f.tr.	0
Id–0 (6)	0	11·9	+93	8·9	f.tr./±	±	0/±	±
Id–1 (6)	0·12	12·1	+105	6·6	0/±	f.tr.	0/tr.	0
Id–2 (6)	0·36	11·8	+100	5·8	0/±	0	0/tr.	0
IIa–0 (6)	0	6·7	+10	9·0	++/++++	+++	0/+	tr.
IIa–1 (8)	0·12	6·7	+10	8·7	+/++	+±	0/+	tr.
IIa–2 (6)	0·36	7·0	+12	7·7	+/++++	++±	0/tr.	0
IIb–0 (8)	0	9·7	+55	6·7	±/++	+	0/±	tr.
IIb–1 (8)	0·12	10·4	+63	5·8	tr./+±	+	0/±	0
IIb–2 (6)	0·36	10·4	+58	5·8	f.tr./+±	+	0/±	0
IIc–0 (6)	0	11·0	+49	10·7	+/+++	++±	0/+	±
IIc–1 (8)	0·12	11·4	+52	9·3	±/++++	+++	0/++	tr.
IIc–2 (6)	0·36	10·1	+46	8·4	tr./+++	++±	0/v.f.tr.	0
IId–0 (8)	0	13·7	+102	7·9	v.f.tr./±	tr.	v.f.tr./tr.	v.f.tr.
IId–1 (8)	0·12	13·0	+109	6·0	f.tr./tr.	tr.	0/v.f.tr.	v.f.tr.
IId–2 (6)	0·36	14·0	+119	5·5	tr./±	tr.	v.f.tr./f.tr.	v.f.tr.
IIe–0 (8)†	0	9·9	+55	27·2	+/++	+ (?)	+++/++++	+++
IIe–1 (8)	0·12	12·0	+67	6·5	0	f.tr.	±/+	±

* The figures in parentheses are the number of rats used in the experiment. f.tr. and v.f.tr. = faint and very faint trace.

† Six out of the eight rats in this group, which were fed the basal diet *unsupplemented* with methionine, died with kidney lesions and fatty livers.

TABLE III.—*Effects of Choline in Diets Inadequate or More Adequate with Respect to Protein*

(Diets IIIa and IIIb contained 3% and 18% respectively, of casein. Diet IV contained 3% protein (2% soya protein plus 1% peanut protein supplied as defatted meal)

Experiment and Diet No.	Choline Chloride (%)	No. of Rats	Average Daily Food Intake (g.)	Average Change in Weight (g.)	Total Lipids (% Liver Wt.)	Lobular Distribution of Stainable Fat	
						Portal	Central
IIIa–0	0	10*	5·7	−12	19·9	+ to ++	++ to +++
IIIa–1	0·50	10*	5·1	−13	5·8	+	±
IIIb–0	0	10*	10·3	+45	23·1	+	++ to +++
IIIb–Opf†	0	10*	6·0	+8	14·3	+ to ++	++ to +++
IIIb–1	0·50	10*	11·1	+60	5·2	±	v. faint tr.
IVa–0	0	10‡	7·0	−75	26·1	+ (?)	+++ to ++++
IVa–1	0·36	15‡	6·3	−74	7·3	±	0
IVa–2	1·0	15‡	6·6	−76	5·8	±	0

* Female rats (65 to 90 g.). † Pair-fed with rats in IIIa–0. ‡ Male rats (180 to 200 g.).

TABLE IV.—*Rate of Appearance of Stainable Lipids in Periportal Areas and Effect on Liver Lipids of Realimentation with an Adequate Diet after a Period on a Similar Ration Low in Protein*

(Forty female rats, 65 to 80 g., fed Diet Va-0 containing 3% casein; pairs of rats killed after periods shown. After 16 days the remaining rats were fed Diet Vb-0, containing 18% casein, for periods shown. Both rations contained 0.54% total methionine and 0.5% choline chloride)

Experiment and Diet No.	No. of Rats	Period Fed (Days)	Average Daily Food Intake (g.)	Average Change in Weight (g.)	Total Lipids (% Liver Wt.)	Lobular Distribution of Stainable Fat	
						Portal	Central
Va-0	2	2	7·1	−2	5·4	+	0 to f.tr.
	2	4	5·6	−10	6·2	0 to +	0
	2	8	5·0	−9	7·1	+ to ++	0
	2	16	4·8	−16	9·1	++	0
Vb-0	8	3	9·6	+19	18·0	+++	0
	8	7	9·3	+38	11·0	++	0
	8	14	10·0	+64	6·3	0 to +	0
	8	21	10·8	+91	5·1	f.tr.	0

moderate loss in weight and resulted in the development of a fatty liver. The total lipids reached 19.9%; there was considerable fat in periportal regions, with even more in centrolobular areas (Plate, Fig. 6). A similar ration containing 0.5% choline chloride resulted in a liver almost free from centrolobular fat but with considerable fat remaining in periportal regions. The total lipids were, however, only 5.8%. Diet Ia-0, a similar ration but with added methionine, was eaten in almost identical amounts and resulted in much lower liver lipids (compare 12.5% with 19.9%), the difference being mainly due to absence of fat from the central areas, as might have been predicted. Diet IIIb-0, methionine-poor but containing 18% of protein, was eaten more freely, permitted a fair gain in weight, and caused a fatty liver, with the abnormal lipids mainly centrolobular, as was anticipated. Paired feeding reduced the total lipids somewhat, but did not change the distribution of stainable fat appreciably. Inclusion of choline chloride (Diet IIIb-1) improved slightly both food intake and gain in weight, and almost completely prevented any stainable fat from appearing in the centrolobular region; a little remained in portal areas.

Experiment IV

Prolonged consumption of a diet low in protein and free from choline produced a very fatty liver, some of the lipid appearing in periportal areas, but most of the abnormal fat being centrolobular (Table III). The centrolobular deposition of stainable lipids was prevented by choline. Thus the effects of a low-protein diet on stainable liver lipids were essentially the same whether the rats were fed for three weeks or three months.

Experiment V

Development of a fatty liver upon realimentation has been noted frequently (for example, MacFarland and McHenry, 1945; Best, Lucas, Patterson, and Ridout, 1951), but the distribution of stainable fat in the present experiment proved interesting, being exclusively periportal. The low-protein diet (3% casein) resulted in a decreasing food intake (Table IV), in spite of adequate vitamins (including choline) and methionine. Despite the diminishing caloric intake and consequent loss of weight, the livers became increasingly fatty, the deposition of fat occurring in periportal regions (Plate, Fig. 7). When the rats were transferred to a similar diet in which the protein was made more adequate (casein 18%) they ate twice as much and began to gain weight. Coincident with this sudden increase in food consumption during the first three days on the "curative" ration there was a dramatic increase in the total liver lipids (to 18%), all of it occurring in periportal regions (Plate, Fig. 8). With continued intake of about the same amount of food, however, the abnormal fat soon disappeared, the liver appearing normal both histologically and chemically at the end of three weeks. No such increase in liver lipids occurred following realimentation in rats pair-fed a commercial ration throughout both the period of decreasing food intake and of realimentation.

Discussion

The data presented above show that protein inadequacy leads to the prompt appearance of stainable fat in periportal regions of the liver. It is a well-established fact that choline deficiency results in a rapid accumulation of abnormal lipids, mainly glyceride in nature, in centrolobular areas; the present data confirm this. The essential difference in the lesions can best be recognized when the deficiency is of mild degree and of brief duration; more severe or more prolonged deficiencies lead to a more generalized distribution of stainable fat, often obscuring the original site of appearance of the lipid.

DESCRIPTION OF SPECIAL PLATE

Photomicrographs (×133) of frozen sections of rats' livers stained with oil red 0 to demonstrate fat.

FIG. 1.—Livers of young rats (Wistar) fed the stock ration ("master fox chow"). In our strain under these dietary conditions there is usually no stainable fat (Fig. 1*a*), but occasionally some cells contain fine droplets and a few are filled with fat. When present these fat-filled cells are distributed at random within the lobule (Fig. 1*b*).

FIG. 2.—Lipid distribution typical of rats fed rations low in protein (made adequate with respect to methionine): Fig. 2*a* without choline (Diet Ia-0), and Fig. 2*b* with supplementary choline (Diet Ia-1). The choline is without significant effect on the periportal fat (++ to +++).

FIG. 3.—In the livers of rats fed Diet IIa-0 (soya protein 9%) there is abundant periportal accumulation of fat (++ to ++++). This photomicrograph illustrates the mode (+++).

FIG. 4.—The periportal deposition of lipids was the least when fibrin (Diet IIb-0) was the protein fed. The figure illustrates the appearance of the liver when the ration is supplemented with choline (Diet IIb-2). The findings (+) are essentially the same in the absence of choline.

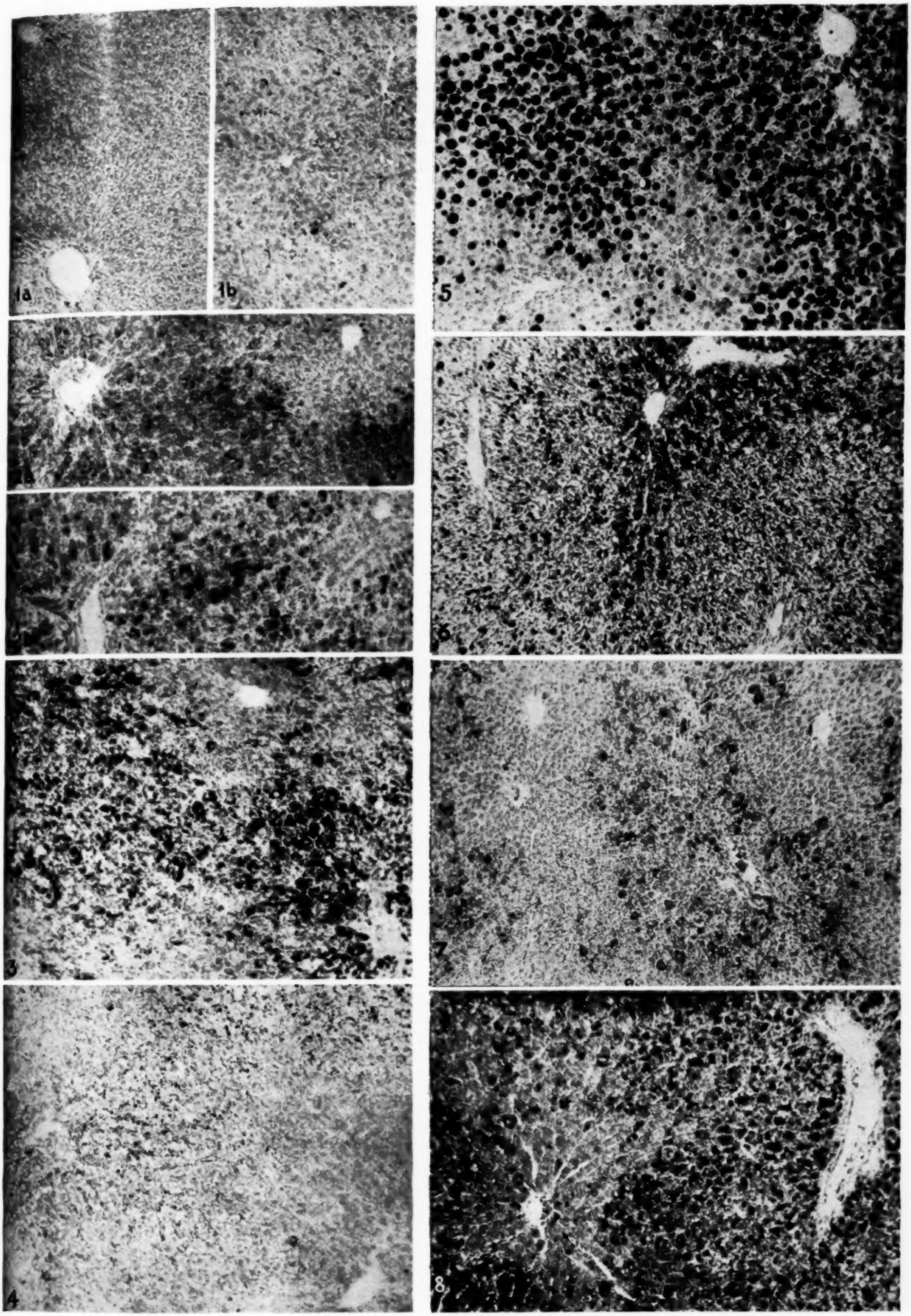
FIG. 5.—Stainable fat in relatively large amounts (+++ to ++++) present in centrolobular and non-portal regions of livers of rats fed rations low in choline (Diets IIe-0 and IVa-0).

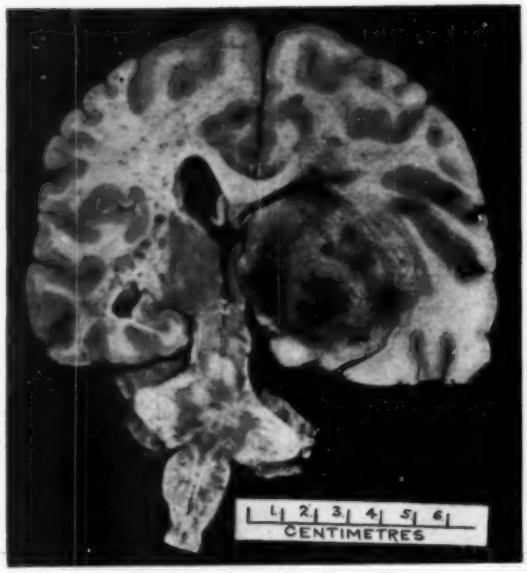
FIG. 6.—Dual distribution encountered in rats fed rations low in both choline and protein (for example, Diet IIIa-0): stainable fat present in relatively large amounts (++ to +++) in centrolobular regions of the liver, and in smaller quantities (trace to +) in periportal areas.

FIG. 7.—Stainable fat (+) present in periportal regions only. Rat consumed a low-protein ration (Diet Va-0) supplemented with both choline and methionine for 16 days; food intake was low. A portal field is just to the right of and below centre.

FIG. 8.—Abundant stainable fat present in periportal fields, but none occupies cells around central veins (one at left). A portal triad, cut longitudinally, is shown on the right. Rat consumed for three days excessive amounts of a ration containing 18% casein (methionine and choline believed adequate—Diet Vb-0). For 16 days previous to the three-day period the rat had eaten only small amounts of the same ration (Diet Va-0) as that consumed by the rat whose liver is shown in Fig. 7.

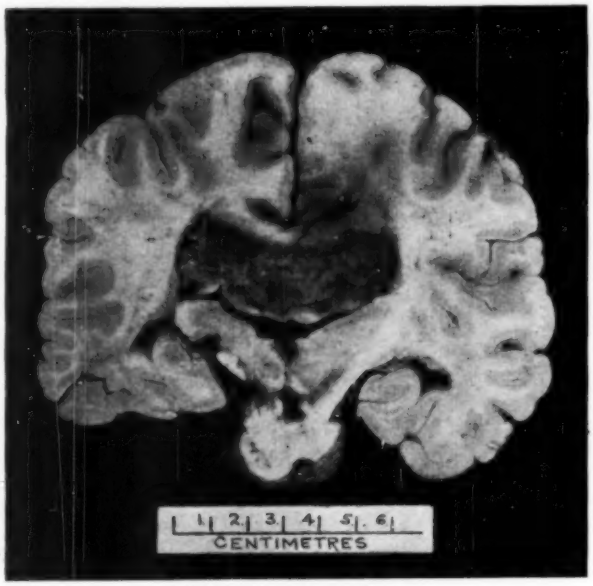
C. H. BEST *ET AL.*: HEPATIC LIPIDS



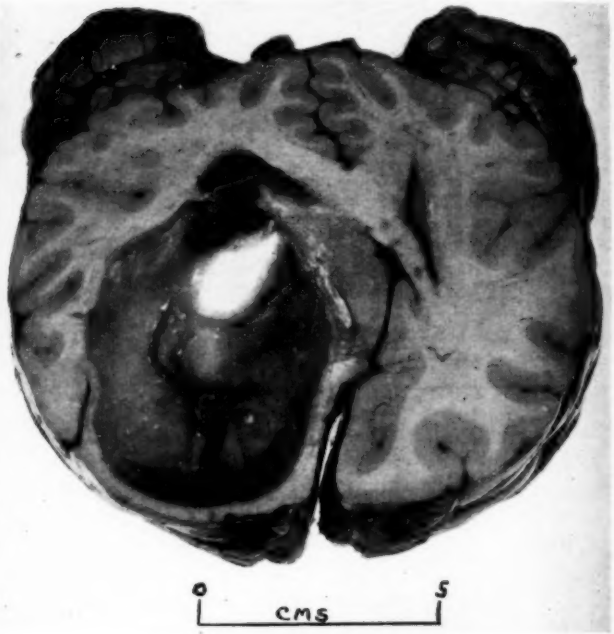


Glioblastoma of basal ganglia.

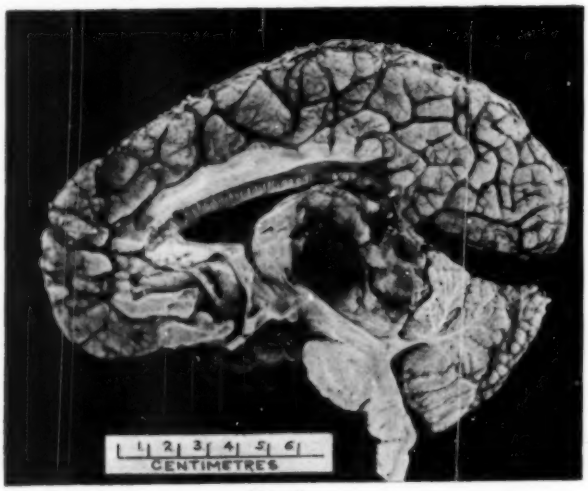
Rapidly growing malignant glioma.



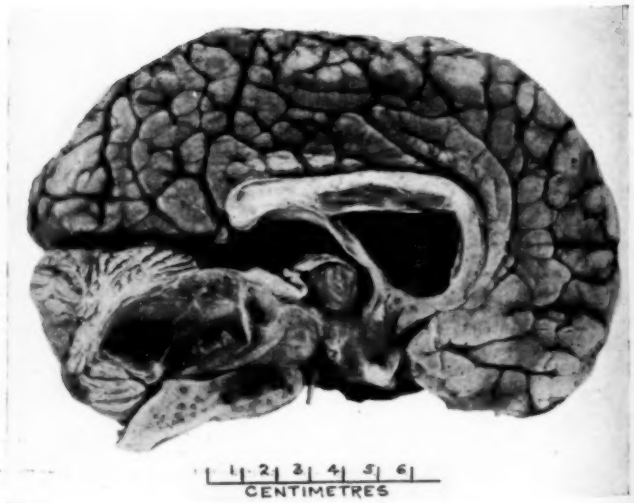
Glioma of corpus callosum.



Astrocytomatous cyst of a hemisphere.



Pinealoma.



Cystic astrocytoma of cerebellum.

For complete protection of the hepatic cells in the portal region the amount of protein necessary depends upon its nature, fibrin being much more effective than casein, which is better than soya protein. The deleterious effect of diets low in protein on the cells in the portal region may be related to some inadequacy of essential amino-acids (cf. Lucas and Ridout, 1955). The effect of protein on hepatic cells around the central veins appears to be attributable largely, if not solely, to its content of the choline precursor methionine. Protein inadequacy in regard to protection of the liver appears to begin at about 12% in the diet when casein is fed, and below 6% in the case of fibrin (cf. data of Winje *et al.*, 1954); choline inadequacy begins at about 0.12% (expressed as chloride). It should be emphasized that these values may vary considerably, depending upon the strain, age, and sex of the rat, upon the adequacy of the diet with respect to other essential nutrients, upon environmental temperatures, and on other factors less well understood.

These observations may help to resolve two anomalies in the literature—namely, the occasional discrepancy between the chemical and histological estimations of liver fat and the lack of response of certain types of dietary fatty livers to the lipotropic agents. The term "fatty liver" has somewhat different connotations according to the viewpoint of the user. To the pathologist who is concerned with the appearance of the organ the liver is described as fatty if fat is evident microscopically in suitably stained sections. Not every cell need contain stainable fat. Cells in certain regions only may be affected, yet the organ would be referred to as a "fatty" liver. The biochemist, on the other hand, is concerned with the results of the chemical analysis—that is, with the quantity of lipids extractable from the tissue. Only when the analytical figure is increased appreciably above the normal range of values for the species would the chemist describe the liver as "fatty." The pathologist may see stainable fat, sometimes in considerable amount, before there is any significant increase in the extractable lipids. An erroneous impression of the magnitude of the increase above normal may be obtained unless attention is paid to the extraction procedure used, and especially to the base to which the analytical data are calculated, whether it be to fresh tissue, dry tissue, fat-free tissue, or dry, fat-free tissue. We have discussed elsewhere the merits and disadvantages of each of these (Ridout *et al.*, 1952). There are situations—for example, in protein depletion—where the values might better be expressed as percentages of body weight, or, better still, referred to the desoxypentosenucleic acid (D.N.A.) content of the liver. Campbell and Kosterlitz (1948, 1950, 1952) found that, although ribonucleic acid and phospholipid are lost from the liver in protein deficiency, the D.N.A. content of the liver of the adult rat varies linearly with body weight and is not affected by the protein content of the diet. Where effects of variations in dietary protein are under study, and particularly where a considerable change in the number of functional liver cells is apparent (as in necrosis or cirrhosis), the D.N.A. content of the liver should prove a useful basis for comparing changes in lipids and other hepatic components. However, at present in our laboratory the common practice is followed of referring the data to the fresh weight basis. All values are also calculated to the dry, fat-free basis, as this sometimes permits more useful comparisons, but these data are not always reported.

In choline deficiency hepatic lipid values of 15 to 40% of fresh liver weight are commonly observed. Figures of 25 to 45% reported in rats fed diets low in protein (for example, Harper, Benton, *et al.*, 1954) are expressed as percentages of *dry* liver weight. When referred to the fresh weight the total hepatic lipids are no more than about 8 to 18% (usually below 14%). These are certainly fatty livers, but quantitatively they are of mild degree as compared with those seen in choline deficiency. A considerable amount of stainable fat may appear in periportal areas with minimal elevation of total lipids as determined chemically. It has been suggested (Lucas and Ridout, 1955) that this unmasking of normal structural lipids (fat phanerosis)* may be caused by improper formation of lipoproteins due to protein deficiency. Protein deficiency may seriously interfere with the formation of many vital factors which the lack of choline might not affect to the same extent. (Cf. Campbell and Kosterlitz, 1948, 1950, 1952.) While fibrosis or cirrhosis has not yet been produced in our rats by protein deficiency in the presence of abundant choline, even after a year, it is possible that these lesions may appear in more prolonged experiments, as Ramalingaswami (1954) has suggested.

With regard to the second anomaly, our findings confirm and supplement those from other laboratories that fatty livers due to diets low in protein do not respond to lipotropic substances. However, it is not surprising that a fatty liver due to protein deficiency is not cured by giving supplements of choline or its precursors.

In our opinion it has been obvious for many years that the clinical use of choline and methionine to repair the liver damage produced by multiple deficiencies—that is, of protein, minerals, vitamins, etc.—is doomed to failure because most hospital diets supply an abundance of the lipotropic agents. This does not decrease in any way the potential clinical significance of experimental work on the lipotropic factors; it merely means that in the laboratory it is possible to make choline the limiting factor by the design of the experiment. The clinician rarely encounters so simple a situation. If he supplied the missing amino-acids other than methionine and made good the other deficiencies except that of choline, this substance would be the limiting factor in the clinical situation.

The importance of the balance of amino-acids in the diet in the study of fatty livers was noted in this laboratory 10 years ago by Beveridge, Lucas, and O'Grady (1944, 1945), who pointed out that the lipotropic activity of a protein is determined not only by its content of methionine but also by the nature and quantity of the other amino-acids present. While studying changes in liver composition during protein depletion Wang *et al.* (1949) fed protein-free rations to rats and observed a fatty liver not completely preventable by choline (at the dosage used, which was high—0.50% choline chloride in the diet). Dick, Hall, Sydenstricker, McCollum, and Bowles (1952) suggested that some fatty livers may result from failure of certain cell functions when protein anabolism is reduced—that is, they may represent a non-specific effect of protein deficiency rather than a specific lack of any one essential amino-acid. When Harper, Benton, *et al.* (1954) observed an anti-lipotropic effect of methionine in rats fed threonine-deficient diets containing choline, they too concluded that the extent of fat deposition in the liver depends on the balance as well as on the absolute amounts of amino-acids in the ration. The fatty livers caused by diets deficient in threonine and lysine (Dick *et al.*, 1952; Singal *et al.*, 1953; Harper *et al.*, 1953), even with moderate amounts of choline in the food, are examples of fatty livers of non-specific origin—that is to say, due to inadequate or imbalanced protein—and the lesions would doubtless prove to be periportal in distribution. Indeed, Niño-Herrera, Harper, and Elvehjem (1954), reporting upon the histological differentiation of fatty livers produced by threonine or choline deficiency, stated:

> "In the livers of choline-deficient animals the fatty infiltration is diffuse and is most severe in the vicinity of the central vein. In the livers of animals receiving low-protein diets containing choline the distribution of fatty cells results in a network appearance in which zones of normal cells are interspersed among the zones of fatty cells and only occasionally is the fatty infiltration not

*This is not the place to attempt a full discussion of the vigorously debated subject of lipophanerosis. Modern biochemical and physicochemical studies of the lipoproteins have revealed the possibility of dissociation of these compounds to give free lipids, but the conditions governing this process are not well understood.

severe around the central vein of the lobule. The magnitude of the fatty infiltration is much greater in rats fed a diet deficient in choline."*

Shils and Stewart (1954b) have observed a periportal distribution of fat in livers of rats fed diets consisting principally of corn meal, rice, or cassava, and found that lysine and tryptophan prevented this fatty liver. These observations are in agreement with our hypothesis that protein deficiency or amino-acid imbalance causes the periportal type of lesion.

Shils and Stewart (1954a) suspected that the periportal accumulation of lipids seen in rats fed corn meal may be due to some unique property of corn proteins. Since the lesion was later seen in rats fed corn, rice, wheat, or cassava, Shils, Friedland, and Stewart (1954) believed that it is typical of plant products. Our finding of this periportal type of distribution whenever the amount of dietary protein is low, regardless of the source of the protein fed, confirms and extends their results but alters the conclusions.

Shils and Stewart (1953) reported observing a sex difference in the distribution of stainable fat in the liver lobule: in male rats the total concentration of hepatic lipids was higher than in females and the lipid appeared first in periportal areas; in females the fat was found first in central areas. Female rats responded somewhat to threonine; males did not (Shils and Stewart, 1954b). In our experiments, admittedly with different proteins, we have not noticed any significant difference in the distribution of stainable fat in the livers of male and female rats.

In a personal communication Ramalingaswami, who with his colleagues has published several thoughtful and stimulating papers on liver injury in protein malnutrition (for example, Sriramachari and Ramalingaswami, 1953; Ramalingaswami *et al.*, 1954), has informed us that the fat content of diets low in protein and choline may influence the localization of the fatty deposits in the hepatic lobule. After rats were fed for about three months on a low-fat, low-protein, choline-deficient diet he observed that the microscopical appearance of the livers presented a striking similarity to the picture in kwashiorkor.

In our present study the observation that may be of greatest practical significance concerns the abrupt increase in total liver lipids associated with a sudden improvement in the quality and quantity of food intake, even when the "curative" ration is adequate in protein and rich in choline (Experiment V). Liver fat increased within three days from 9 to 18%, all stainable fat being present in periportal regions. This is the largest amount of extractable lipid ever observed by us when the stainable fat was present in periportal regions exclusively. A similar increase in liver fat was not observed in other rats pair-fed a commercial stock ration, suggesting that an unidentified factor prevents the sudden but transient increase in liver lipids confined to the periportal regions. These experiments, which may have their clinical counterparts in the treatment of alcoholic subjects with certain "good" diets, reveal the presence of factors in addition to protein and choline that may be concerned in the deposition and localization of fat in the liver.

Summary

In rats fed diets containing a moderate amount of fat and 9% or less of protein, supplementary choline failed to prevent completely the accumulation of fat in periportal regions of the liver.

Lack of adequate protein resulted in the appearance of fat in the periportal areas, while deficiency of choline (or precursors) caused an accumulation of fat in the cells bordering on the central vein. Protein inadequacy has not produced the massive accumulation of hepatic lipids seen in choline deficiency.

When rats were transferred on to an "adequate" diet (containing 18% casein and 0.5% choline chloride) after a period on a low-protein ration (3% casein) there was a dramatic appearance of a transient fatty liver (total lipids 18%), the fat appearing in periportal positions only. During three weeks on the same ration the hepatic lipids returned to normal. Other rats pair-fed the same amounts of a commercial ration did not develop fatty livers, so that the transient appearance of periportal fat is not entirely due to the increased food intake. Certain points of potential clinical interest have been discussed briefly.

The expenses of this study were defrayed in part by a grant to the Department from the Banting Research Foundation. Our thanks are due to Mr. Gwen Hughes, of the Charles Albert Smith Co. Ltd., Toronto, and to Distillation Products Industries, Rochester, N.Y., U.S.A., for a generous donation of pure α-tocopheryl acetate.

We wish to thank Dr. W. G. Bruce Casselman and Dr. Jean M. Patterson for the exceptional amount of help they have given us in this study.

(A preliminary account of some of these findings was read at the 37th Annual Conference of the Chemical Institute of Canada, Toronto, June 21 to 23, 1954.)

*The literature concerning the site of lipid accumulation in threonine deficiency is contradictory, however. Dick and his associates reported that it occurs in the cells around the central veins. Unfortunately the histological techniques used by Niño-Herrera *et al.* were unsuitable for lipid studies. Using histochemical methods, Kerbel and Casselman in this laboratory have repeated the experiments relating directly to threonine deficiency and have found that the distribution of fat is clearly periportal.

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In 1953 in England and Wales 40 people were killed in quarry accidents and in Scotland 5. In 1952 these totals were 49 and 4 respectively. The injured numbered 104 in 1953 in England and Wales and 11 in Scotland, as compared with 118 and 14 respectively in 1952. The average death rate per 1,000 persons employed in all quarries in England, Scotland, and Wales was 0.99 in 1951, 0.85 in 1952, and 0.73 in 1953.—*Report of H.M. Inspectors of Mines and Quarries for 1953* (H.M.S.O., 2s.).

THE PROBLEM OF GLIOMA OF THE BRAIN*

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[WITH SPECIAL PLATE]

There tends to be a periodic lack of interest in the study of cerebral gliomata, though these neoplasms continue to inflict their havoc on the health and lives of far too many young and middle-aged people. This paper is therefore aimed at recalling attention to this important subject and reviewing certain facts and conclusions gained from our experience with a consecutive series of 700 patients with neoplasms of the brain, of which 466 were gliomata.

Surgical Pathology

The gross post-mortem appearances of gliomata are usually so distinctive that these neoplasms can be differentiated almost as well by the naked eye as by histological examination. Of the 466 gliomata in our series, 294 were completely solid and 172 partly cystic. In only 20 of the cystic cases was the neoplasm composed of a large cyst and a relatively small amount of tumour; in the other 152 the cysts were small in relation to the solid mass of the tumour.

The gliomata were classified histologically according to cell type as originally suggested by Bailey and Cushing (1926), this work being carried out by the late A. F. Bernard Shaw, Professor of Pathology in the University of Durham, and also by Professor R. Paterson Smith. The results were as shown in Table I.

In the unclassified group were placed neoplasms the histological appearances of which did not strictly conform to the criteria of diagnosis laid down by Bailey and Cushing: most were highly malignant. Even the most typical of the astrocytomata and oligodendrogliomata were not composed of a uniform type of cell; in the highly malignant types one zone differed considerably in cell content, cell size, mitotic activity, and vascularization. In no instance was it possible from the histological studies to reconstruct the general architecture of the growth and the way in which its mass was given cohesion. There were areas which seemed to be without any kind of histological pattern and yet did not appear to be zones of necrosis or of haemorrhage. A discrete edge to a glioma was never seen; brain tissue apparently reacts but little to the advance of a glioma. Cells presumably neoplastic in nature can nearly always be seen at considerable distances from, and entirely unconnected with, the main mass of the neoplasm.

*This paper was submitted for publication in December, 1952.

TABLE I

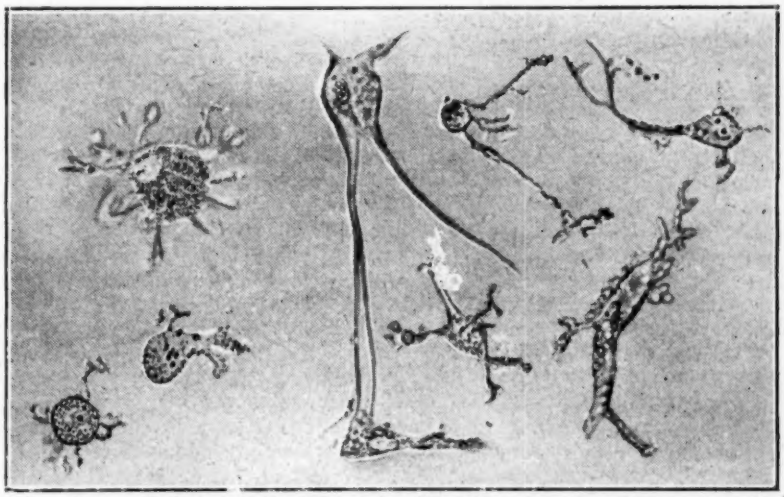
Type of Glioma (See Special Plate)	Adults	Children (Up to the Age of 12)
Astrocytoma:		
(*a*) Hemispheral	54	2
(*b*) Cerebellar	9	6
Astroblastoma	10	2
Spongioblastoma unipolare	5	2
Glioblastoma (spongioblastoma multiforme)	76	1
Oligodendroglioma	9	—
Ependymoma	7	6
Medulloblastoma	9	21
Haemangioblastoma	5	—
Pinealoma	3	2
Unclassified:		
(*a*) Partly cystic	66	2
(*b*) Solid	156	11
Papilloma	2	—
Total	411	55

As the appearance of a cell after it has been prepared for histological examination cannot possibly resemble that of its natural state, an effort was made to grow specimens in culture. This work was first carried out at the Christie Hospital and Holt Radium Institute, Manchester, with the help of Dr. Edith Ralston Patterson. The accompanying drawing, made by Miss D. Davison, depicts what was seen through a microscope at the edge of a culture of a glioblastoma.

There is now a tendency to classify gliomata according to their degree and type of malignancy. Theoretically this method may be an advance on the classification by cell type; in practice, however, it is doubtful whether it has any advantages, because, although precise criteria for classification can be laid down, tumour variations are so great that strict grouping according to the accepted rulings is difficult.

In the 231 cases in which the glioma was given a formal name the sites of occurrence were: frontal lobe, 49; temporal lobe, 66; parietal lobe, 44; occipital lobe, 12; third ventricle, 8; fourth ventricle, 6; brain-stem, 5; cerebellum, 41. In some instances the neoplasm was too large to be certain of the structure from which it originated, although it is obvious that most of the malignant types arose in the basal ganglia, vermis of the cerebellum, or corpus callosum. Also, although the bulk of many neoplasms occupied one lobe of the brain, extension had taken place into neighbouring zones. In no instance was there a metastasis outside the central nervous system.

The age incidence was as follows: 1 to 12 years, 42; 13 to 19, 18; 20 to 29, 31; 30 to 39, 43; 40 to 49, 44; 50 to 59, 44; 60 to 69, 9.



The microscopical aspect of cells growing from the edge of a culture of a glioblastoma. These appearances no doubt conform to the normal characteristics of cells before subjection to the processes of histological preparation.

The Problem of Early Diagnosis

In a case of cerebral glioma the clinical picture of course depends substantially on whether the neoplasm is in the early or the late stages of development. Moreover, in view of the many and widespread structures from which a glioma may arise, it will be obvious how difficult it is to consider a diagnosis without first grouping these neoplasms according to type and then subgrouping the types according to site of origin. For example, the clinical picture of cystic astrocytoma of the cerebellum is very different from that of astrocytomatous cyst of a hemisphere. Nevertheless this apparent need for subgrouping leads to a tendency to await a fully developed clinical syndrome before a firm diagnosis of cerebral neoplasm is risked. Late diagnosis may not be greatly detrimental therapeutically where a glioma is concerned, but has serious consequences in the case of meningioma or acoustic neuroma.

Here, in the interests of earlier recognition of a neoplasm, we will attempt to discuss diagnosis from the first symptom or sign in the group as a whole, without segregating the tumours into subgroups—for example, cystic astrocytoma of the cerebellum and the glioblastoma of the hemispheres. In the 231 cases in which the neoplasm was given a formal name we were able to classify the initial symptoms or signs as follows:

1. *Rise in Intracranial Pressure.*—In 142 instances headache, vomiting, dizziness, and papilloedema, singly or in combination, were the first signs or symptoms. Papilloedema was an early sign in 10 cases only, and, of course, was pathognomonic of a space-occupying lesion. In the remaining 89 cases a diagnosis was impossible on the characteristics of the headache, dizziness, or vomiting.

2. *Epilepsy.*—A sudden attack of epilepsy was the first sign in 40 cases; in 38 of these the seizures were major, and in the remaining 2 focal. All the attacks occurred in patients between the ages of 20 and 60 years. In 6 cases the seizures were followed by neurological signs from which the patient never fully recovered; in 4 cases there was hemiparesis, and in 2 a mild dysphasia. In every instance a lesion other than a glioma, or even a neoplasm, could have been the cause.

3. *Mental Change.*—Although in only 15 out of the 231 cases did mental change herald the presence of a cerebral glioma, it is probable that in many cases this symptom was overlooked or its significance not appreciated. Initially, mental change leads to minor and very subtle changes in behaviour that can be elicited only by direct questioning of an intimate relative or friend. A common first sign is a carelessness about personal appearance—for example, a man hitherto fastidious about his appearance may fail to shave cleanly, or a woman usually scrupulous about her hair may leave it unbrushed and untidy; again, a normally punctual person may start to get up late and show no concern about prompt arrival at work. Every change in behaviour cannot, of course, be regarded as having a sinister meaning. An intimate relative is quick to detect deterioration, but often withholds the information if not directly cross-questioned. The assessment of a minor change in behaviour makes heavy calls on the good judgment and experience of a general practitioner. Frank mental confusion and gross faults in behaviour, such as incontinence, are later signs of mental deterioration. Mental signs may, of course, be due to many kinds of pathological change, and when present can merely call attention to the possibility of a cerebral tumour and no more.

4. *Abnormal Neurological Signs.*—The appearance and persistence of an abnormal neurological sign was the first evidence of neoplasm in 34 of the 231 cases. All these signs, some of which developed rapidly and some slowly, could obviously have been caused by a lesion other than a tumour. They are as follows: hemiparesis, in 16 cases; dysphasia, 9; squint, 4; sensory loss, 2; ataxia, 3.

Differential Diagnosis

It will be apparent, therefore, that in most cases of glioma it is impossible to make a diagnosis on the first symptom or sign. Often it is difficult even to decide whether or not the brain itself is primarily affected. Also, to make diagnosis more difficult, other space-occupying lesions present more or less in the same way. In our series, for example, the gliomata had to be differentiated not only from vascular and degenerative lesions of the central nervous system, but from other types of space-occupying lesion, as shown in Table II.

TABLE II

Diagnosis	Adults	Children (Up to the Age of 12)
Glioma	411	55
Secondary carcinoma	62	—
Meningioma	59	2
Acoustic neuroma	25	—
Tumour of pituitary body or stalk	61	6
Epidermoid (cholesteatoma)	5	—
Granuloma	7	7
Total	630	70

In the few instances when the first symptom or sign throws strong suspicion on the possibility of a cerebral neoplasm it is probably wiser to proceed with special neurological investigations to establish diagnosis than to await the development of further confirmatory symptoms or signs. In the majority of cases, however, it is necessary to await possible developments before it can be decided that one is dealing with a progressive lesion of the central nervous system. But it is absolutely wrong to await the development of a fully established clinical syndrome before making a diagnosis or applying special diagnostic tests. For example, it is not necessary, in the case of a man who is forgetting an occasional word, to defer a diagnosis of glioblastoma until he is completely aphasic, disorientated, incontinent, and going blind with papilloedema. At the same time to swing violently from the policy of overwaiting to mere mechanistic methods of diagnosis is equally unsatisfactory. Obviously a multitude of patients with minor and purely transient disorders should not be subjected to the discomforts and dangers of special neurological investigations, nor should the usual simple clinical tests to eliminate conditions such as nephritis and hypertension be omitted.

Special Diagnostic Methods

Although straight radiographs of the head rarely reveal anything abnormal in the early stages of a space-occupying mass in the brain, they do occasionally show signs of pressure, hyperostosis, erosion, calcification, or dislocation of the pineal gland, and therefore should be made use of, particularly as this form of radiography is painless and without danger. Electroencephalographic investigation is also painless and without risk, and should be used routinely in the detection of neoplasms in their early stages. We have found electroencephalography to have limited value, however, as it tends to establish that a physical lesion is present without giving precise information concerning its pathology; but this should not preclude its free use.

Lumbar puncture may show that intracranial pressure is raised before there is clinical evidence of it. Occasionally a rise in the protein content of the cerebrospinal fluid is the first positive evidence of a cerebral tumour. In the early stages of a space-occupying lesion the value of lumbar puncture far outweighs its possible dangers.

When, in spite of the procedures referred to above, diagnosis is still in doubt, air encephalography, ventriculography, or cerebral angiography will be necessary to decide whether a neoplasm is present, and, if so, its nature.

In our experience, where there is little evidence of a rise in intracranial pressure, air encephalography is perfectly safe and is one of the most reliable methods for detecting a space-occupying lesion of the brain. Although we have performed air encephalography many hundreds of times during the last ten years we have not had one fatality or seen a single complication as a result.

Ventriculography is the safer method of air or oxygen replacement when there is obvious evidence that the intracranial pressure is raised. This procedure involves making two holes in the skull through which cannulae can be passed into the lateral ventricle, whereas with air encephalography it is necessary only to tap the spinal theca with a hollow needle at the lumbar or cisterna magna level.

Cerebral angiography is a most important procedure, by the aid of which it is possible not only to determine with great precision whether a space-occupying lesion is present and, if so, its location, but also to obtain valuable information concerning its pathology.

Neither cerebral angiography nor ventriculography is to be carried out lightly, as considerable danger is involved.

Operative Treatment

It is our purpose to summarize briefly the surgical methods of treatment we have employed in this series of 466 cases of glioma, of which 405 were operated upon, and to review our main surgical conclusions.

1. When once a cerebral tumour has been firmly diagnosed in its early stages, and provided the intracranial pressure is not high, no effort should be spared to establish its precise location and pathological nature, if necessary by air studies and angiography.

2. Burr-hole inspection and probing we have found to be useful in diagnosis for excluding chronic subdural haematoma or intracranial abscess, but taking a biopsy specimen through a burr-hole we have found to be of little value and often dangerous.

3. In the later stages of a cerebral neoplasm, when the intracranial pressure has been obviously high, we have often dispensed with air studies or angiography and chosen the site for exploration on the evidence of clinical symptoms and signs. Nowadays the removal of an osteoplastic flap for exploration of a tumour through the dura mater is a relatively benign procedure; it is often safer, quicker, and less dangerous to the patient than ventriculography or angiography.

4. To plan an exploration over the vault of the skull or in the posterior fossa merely to uncover a tumour without also taking into account the anatomical peculiarities of the area concerned will usually lead to unnecessary technical complications; for example, radical operations in the area of the frontal fossa are difficult unless the osteoplastic flap has been cut close to the edge of the superior longitudinal sinus and down to the floor of the frontal fossa. In operations in the area of the posterior fossa an angle tumour cannot be approached adequately through a midline exposure.

5. When operating to remove one of the more benign types of glioma the excision should be as radical as possible but without inflicting damage on those areas of the brain that must inevitably lead to severe incapacity. For example, we regard the surgical imposition of a hemiplegia as worse than failure.

6. Experience has taught us that piecemeal removal of a glioma is a waste of time. The only worthwhile type of internal decompression is the formal resection of a block of cerebral tissue—for example, excision of that part of the frontal lobe of the brain that lies within the anterior fossa.

7. Subtemporal decompression is to be avoided at all costs. For the last ten years it has been our practice, even if an osteoplastic flap is raised, never to open the dura mater unless there is reasonable certainty that it can be closed again; in other words, operability must be determined by the appearance of the brain through the dura mater or by probing. First to open the dura in the hope of being able to do something useful operatively will in only too many cases lead to the development of unsightly bulges on the head due to cerebral herniations.

8. When a diagnosis of malignant glioma can be established beyond reasonable doubt, a surgeon is justified in refraining from operating. With the help of special investigations, particularly cerebral angiography, a reasonably certain diagnosis can often be arrived at.

Prognosis

It will have been seen from the section on surgical pathology that every glioma is malignant. Indeed, the majority of gliomata are highly malighant and grow so quickly that they cause serious incapacity within a few months, and death within two years. A small percentage of neoplasms at the astrocytomatous end of the scale are relatively benign and may continue to grow for 10 to 20 years before fatally compressing the brain-stem. Some tumours, such as the cystic gliomata and haemangioblastomata of the cerebellum, although not naturally self-limiting, are so circumscribed that they can be totally excised and the patient cured. However, in the large majority of cases surgery cannot offer cures, and, this being so, it might with reason be asked why a neurological surgeon so often operates on the gliomata. Indeed, the taunt that his persistent efforts at surgical cure in these cases reveal "the triumph of optimism over common sense" has often been levelled. There is no doubt to prolong a patient's life in misery is poor surgical judgment. None the less, despite his knowledge and experience, a surgeon is often compelled to operate against his better judgment, by pressure of relatives or colleagues or by the uncertainty of the pathological diagnosis.

In reviewing the results of the operative treatment of gliomata a broad perspective must be maintained. For example, a patient's life can easily be prolonged by a wide but unsightly subtemporal decompression. In this connexion it might be asked what are the ethical responsibilities of a surgeon. His main object is, of course, to cure the patient or to relieve severe symptoms which are unaffected by simpler methods. However, a surgeon is quite entitled not to interfere with natural processes where he is confident he cannot favourably alter their course by his intervention. The more experienced a surgeon becomes the less frequently is he inclined to operate on gliomata.

Results

The results in our series have been as follows:

Cures.—Seven patients have been completely cured; in this group were 2 cases of haemangioblastoma and 3 of cystic astrocytoma of the cerebellum, and 2 of mucous cyst of the third ventricle.

Substantial Prolongation of Useful Life.—Twenty-three patients who were already completely incapacitated by the effects of cerebral compression were returned to useful life for the following periods: 4 with cystic glioma of the cerebellum, 5 years; 2 with oligodendroglioma of the frontal lobe, 5 years; 10 with cystic astrocytoma of a hemisphere, 2 years; and 7 with oligodendroglioma of a hemisphere, 2 years.

Substantial Relief of Symptoms.—In 52 cases distressing symptoms, such as severe pain and intractable vomiting, were relieved by operation when drugs, other than those interfering with consciousness, were of no avail.

Deep *x*-ray therapy, although found to retard the rate of growth of some of the more highly malignant of the gliomata, was never curative.

Conclusions

Though surgery has little to offer in the cure of cerebral gliomata, the diagnosis of these neoplasms, the care of patients suffering from them, and the management of near

relatives still remain the onerous responsibility, and the duty, of those doctors who choose to make the problem of cerebral neoplasia one of their primary interests. Moreover—and this is even more important—in our series of 700 unselected cases of cerebral neoplasm, although 466 were gliomata, there were 147 cases that were potentially curable by surgery; in other words, 21% of favourable cases. In cases of neoplasm of the brain the segregation of the favourable cases from those of glioma in the early stages is one of the main problems of differential diagnosis, and carelessness in the diagnosis and handling of the glioma cases will reflect unfavourably on the potentially curable group.

In a further group of cases we are already using the newer methods of diagnosis, such as with radioactive isotopes, and are experimenting with biochemical forms of treatment and deep *x*-ray therapy.

Summary

Experience with 700 cerebral neoplasms, of which 466 were gliomata, is reviewed.

The majority of these new growths are highly malignant and lead to death within two years. Early diagnosis is important. The initial symptoms and signs are raised intracranial pressure, epilepsy, mental change, and neurological signs, though it is generally impossible to base a diagnosis solely on the clinical evidence. *X* rays, electroencephalography, and lumbar puncture are useful diagnostic aids, but when these fail air encephalography, ventriculography, or angiography will be necessary to decide if a space-occupying lesion is present.

Surgical methods of treatment are summarized and discussed. It is emphasized that subtemporal decompression should be avoided.

Of the 405 patients operated upon, 7 were cured, 23 were returned to a useful life for periods of two to five years, and 52 relieved of distressing symptoms such as severe pain and vomiting.

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REFERENCE

Bailey, P., and Cushing, H. W. (1926). *A Classification of the Tumours of the Glioma Group on a Histogenic Basis with a Correlated Study of Prognosis.* Lippincott, Philadelphia.

The "Mental Health Facilities and Needs of Australia" were the subject of a report drawn up by Dr. ALAN STOLLER, Melbourne psychiatrist, with the assistance of Mr. K. W. ARSCOTT. The report was undertaken at the instigation of the Commonwealth Government and published by it. Its scope included examination of mental hospitals and auxiliary services, mental deficiency programmes, psychiatric services, and State legislation. Dr. Stoller sums up his findings on the hospitals: "Mental hospitals are hopelessly overcrowded, poorly maintained, and short-staffed. . . . Diagnostic and treatment equipment and facilities are sorely lacking. The hospitals are in no position to develop out-patient, training, and educational programmes, and research is virtually unthinkable." The average overcrowding percentage was 20%—at the main mental hospital for Queensland the figure was 95%. Victoria had the best mental health facilities, with active voluntary bodies, and residential centres for defective children. New South Wales provided four psychiatric clinics through the school medical service; elsewhere help for retarded children was extremely limited and legislation for them incomplete, so that often the number of such children was unknown. Early in May the Commonwealth Government announced a £A.30m. capital works programme to improve mental health facilities throughout the country.

BERYLLIOSIS: A CASE REPORT

BY

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The hazards of dermatitis and respiratory disease from handling beryllium compounds were known in Europe before the last war, and Marradi Fabroni (1935) suggested calling the lung disease berylliosis. Various syndromes caused by beryllium were seen in considerable numbers in the United States of America during the last war, and these have been reviewed by DeNardi *et al.* (1953). In Great Britain, beryllium has been used, though not in the same quantities as in America, in the fluorescent lamp industry and in the form of beryllium-copper alloys in the manufacture of electrical equipment and special springs. It is remarkable, therefore, that there has been only one published case of delayed pneumonitis in a beryllium worker in this country (Agate, 1948) and one case of beryllium granuloma of the skin in a fluorescent-light-tube worker (Lederer and Savage, 1954).

The delayed chemical pneumonitis first described by Hardy and Tabershaw (1946) is perhaps the most interesting and elusive manifestation of beryllium toxicity. It is a slowly progressive sarcoid-like change in the lungs and liver which may come on after a very short exposure to beryllium compounds and after a latent period which may vary from a few months to eleven years. The clinical features are the insidious onset of weight loss, weakness, dyspnoea, and cough, with occasional febrile periods. The prognosis is grave, as the mortality in 35 cases reported by DeNardi *et al.* (1953) was 35%, and many of the remainder were severely disabled by pulmonary fibrosis.

The only British case (Agate, 1948) occurred in a physicist working on the development of tubular fluorescent lamps who was exposed to small quantities of zinc beryllium manganese. His symptoms did not develop until three years after his last contact with beryllium.

Although the first cases were described in a fluorescent lamp factory, it has also been reported in a brass foundry making and finishing beryllium-copper alloys (Jackson, 1950), and even in people who lived near beryllium extraction plants. Hardy (1951) lists 11 different industries in which chronic beryllium poisoning has been found. The incidence of chronic berylliosis is fortunately low. DeNardi *et al.* (1953) report 8 cases among 3,027 workers in three beryllium extraction plants, though 6 cases were found in 310 workers in the brass foundry (Jackson, 1950).

The following case is reported to draw attention to the possibility of delayed chemical pneumonitis due to beryllium in an industry hitherto regarded as safe. The case also shows the combination of unusual skin granulomata with lung lesions and would appear to be due to beryllium-copper alloy.

Case Record

A 25-year-old woman was referred to the skin department in August, 1954, for treatment of Raynaud's phenomenon of the fingers, from which she had suffered since the age of 10. It was noted that, as well as having cold blue fingers, she had numerous linear granulomatous papules on the fingers, palms, forearms, and legs (Fig. 1), and that she had a granulating wound on the dorsum of the left foot, which she

FIG. 1 (*Above*).—Leg showing linear sarcoid reaction. FIG. 2 (*Below*).—Patch tests with beryllium salts 48 hours after application.

stated she had cut at work four months previously and which had not healed. The granulomatous papules had appeared in the previous year. She also complained of a dry cough and increasing shortness of breath, which had so worried her that two weeks previously she had attended a mass radiography unit for a chest *x*-ray examination but no abnormality had been found. She had not lost weight, but had felt weak.

At the age of 10 she had had an attack of arthritis which had left some deformity of the right hand. Since the age of 10 she had had Raynaud's phenomenon of the fingers and toes. Her family history showed nothing relevant.

Occupational History.—For eight and a half years she had been employed by a firm of precious-metal smelters. For the first five years she was a backer in the rolling mill, handling gold, silver, and platinum sheets, and for the remaining three and a half years she operated a rotary shearing machine. This machine trimmed metal strip, a considerable quantity of which was 2% beryllium-copper alloy. She sustained frequent cuts and scratches on her hands, forearms, and legs from the sharp and jagged edges of the metal strip, and she could recall that the cut on her foot and several of the other linear granulomatous lesions had been caused by beryllium-copper strip. The machine which she operated was in a room by itself and she had no contact with fumes or dust from any other process. The shearing blade of the machine revolved only slowly, but fragments of the metal were occasionally thrown off.

On examination in August, 1954, she was not dyspnoeic at rest, but slight exertion produced rapid shallow breathing. Her fingers when cold were dusky blue and there was soft-tissue thickening around the right second and third metacarpo-phalangeal joints. On the back of the fingers and in the palms were numerous firm bluish-red papules, mainly aggregated in lines 0.5–1 cm. long. In the palms also were several superficial dry ulcers 2 mm. in diameter which resembled small chrome ulcers. On both forearms and on the lower part of the legs were more papules varying in colour from a yellowish brown on the forearms to a purplish blue on the legs, which showed acrocyanosis. On the limbs the papules had obviously occurred along scratch marks. On the dorsum of the left foot was a healing laceration which showed a granulomatous lupoid change in the scar. No skin lesions were found on the trunk or face. No abnormality could be found in the cardiovascular system, nor were any adventitious sounds heard in the chest. There was no lymph-node enlargement, and the liver and spleen were not palpable.

Investigations

Histological examination of a papule from the left middle finger showed, in the dermis, numerous well-circumscribed nodules separated by dense fibrous tissue. The nodules consisted of foci of epithelioid cells, multinucleated giant cells, and small round cells. There was no caseation. Dark-ground and polarized-light examination of the section showed no foreign bodies. Histochemical staining for beryllium was negative. Mantoux test, 1/1,000 and 1/100—negative. The blood W.R. and Kahn test were negative. A blood count showed: Hb, 96%; white cells, 6,000 per c.mm. (polymorphs 60%, lymphocytes 30%, monocytes 8%, eosinophils 2%); E.S.R., 27 mm. in 1 hour; serum calcium, 9.8 mg. per 100 ml.; plasma proteins, total 7.3 g. per 100 ml. (albumin 4.8 g., globulin 2.5 g.). The E.C.G. was normal. Beryllium in urine, negative; beryllium in skin, negative.

Radiological examination of the hands and feet showed no abnormality. The lung fields showed a generalized very fine stippling; the picture was not the usual one seen in sarcoidosis, in which the stippling is usually dense and the hilar glands are more commonly involved. The evidence seemed to point to these changes being berylliosis rather than sarcoidosis, although differentiation is extremely difficult. Miniature radiographs of October, 1953, and August, 1954, did not demonstrate changes.

Skin patch tests were carried out with 1% and 2% solutions of beryllium sulphate and beryllium nitrate. In 48 hours a strongly positive eczematous reaction occurred beneath all four patches (Fig. 2). The inflammatory reaction was still present three weeks after the tests, and a skin biopsy was carried out from one area. There was a pronounced pseudo-tuberculous reaction in the dermis, made up of groups of concentric follicles. Each follicle was comprised of epithelioid cells, and most contained a multinucleated giant cell, some of these being very large with up to 50 nuclei. In one or two of the deeper follicles there was a necrotic centre. The epidermal changes were not significant. The follicles differed from the usual form of sarcoid in showing the central necrosis. No acid-fast bacilli could be found, nor optically active particles. Patch tests, using the same strength of solution carried out on 113 normal controls, were negative. One hundred of these patch tests were performed at St. John's Hospital for Diseases of the Skin (C. D. Calnan, 1955, personal communication).

Respiratory Function Tests.—Gaensler Timed Vital Capacity:— Total vital capacity, 2.19 litres, which is 75% of the predicted value for her age and weight; percentage of vital capacity expired in the first 0.75 second=75% (normal). Helium mixing:—The rate of diffusion of the helium was slightly abnormal; there was some slowing of diffusion even in the best-ventilated part, and a small volume into which diffusion was slower still.

Progress.—The patient's dyspnoea and cough has become more marked during the three months she has been under observation. For several days after the patch tests the dyspnoea appeared to get worse than usual and moist rales were heard over both lungs for the first time. These have since disappeared. She has been removed from contact with beryllium and has been found a sedentary job which is within her capabilities.

Diagnosis

The presenting feature of sarcoid-like granulomata on skin damaged by beryllium-copper strip suggested at an early stage that at least the skin lesions were being produced by

beryllium, though lesions occurring as a Koebner phenomenon in sarcoidosis could not be excluded. The presence of small indolent ulcers clinically resembling chrome ulcers and previously described beryllium ulcers was, however, much in favour of berylliosis.

In 1953 DeNardi *et al.* reported the reliability of skin patch tests, which, they stated, showed an eczematous contact sensitivity in cases of berylliosis which had never shown any evidence of dermatitis. Patch tests were positive in 12 of their cases of chronic berylliosis, and results were negative in 5 other patients with various lung diseases, including sarcoidosis. The reliability of patch tests is also stressed by Van Ordstrand (1954), who states that, so far, he has no knowledge of a false-positive result. DeNardi *et al.* suggest four criteria upon which the diagnosis should be based: (1) history of exposure to beryllium; (2) clinical course of the pulmonary syndrome, including studies of pulmonary function; (3) radiographic evidence of granulomatosis of the lungs; and (4) patch tests.

The radiographic changes shown are those described by Wilson (1948) as stage I. He states that the earliest recognizable variation from the normal is a fine diffuse granularity presenting a fine sandpaper appearance, which under magnification of a reading-glass suggests a sandstorm. It is of interest that the miniature films taken by the mass radiography unit were incapable of showing this early positive change.

The patch tests were strongly positive, and it appeared that during the height of the skin reactions the lung lesions became temporarily more active. The initial change in the skin beneath the test patches appeared macroscopically to be an eczematous one, but a biopsy was not carried out immediately and there is no histological confirmation of this. Most significant, however, is the finding in the patch-test area three weeks later. Macroscopically the skin was still reddened and scaly and slight induration could be felt. Histologically, a sarcoid reaction was already present, and this extended deep into the corium. Histochemical staining to detect beryllium failed to demonstrate the metal in this tissue. Attempts to demonstrate beryllium in the urine and in skin papules from the forearm were also negative. Although unsatisfactory, there are a number of proved cases of berylliosis with similar negative findings (DeNardi *et al.*, 1953; Agate, 1948; Lederer and Savage, 1954).

Discussion

This case provides additional evidence that it is beryllium itself rather than beryllium in association with silicates which is responsible for the sarcoid-like granulomata of the lungs and dermis. It also supports the theory that berylliosis is an acquired allergy. In favour of the allergy theory are the low incidence among workers exposed to beryllium, the long latent period, and the minute amounts of the metal necessary to produce the disease.

It is difficult to determine in the present case how the beryllium entered the body, since the metal chips from the shearing machine were quite large and not likely to be airborne. That sufficient entered the body to produce an eczematous hypersensitivity is proved by the positive patch tests. It is perhaps strange that the patient did not show a contact dermatitis when handling the beryllium alloy, but the explanation may lie in the fact that metallic beryllium is very insoluble and until it has undergone some change in the body does not produce a response. Aldridge *et al.* (1949) have shown that beryllium ions attach themselves rapidly to protein, and it is likely that a beryllium-protein compound acts as the sensitizing allergen for the skin.

Of great interest was the sarcoid-like change in the dermis three weeks after application of beryllium nitrate solution to the skin. This reaction has not previously been reported in berylliosis. Although sarcoid reactions can be produced in sarcoid patients by the injection of extracts of lymph nodes and by tubercle bacilli and their extracts, I have been unable to discover a previous description of a sarcoid reaction to substances applied to the skin. If the dermis responds to the presence of beryllium in this way, it is possible that the lung responds in the same way and the delayed chemical pneumonitis can thus be explained as an acquired hypersensitivity.

As has been stated, the prognosis of chronic berylliosis is poor and treatment has been disappointing, though there have been reports of benefit from the steroid hormones (Kennedy *et al.*, 1951). In the present case the symptoms are not disabling, and after removal from contact with beryllium the patient has been encouraged to continue working at a sedentary job within her physical capabilities.

Summary

A girl trimming 2% beryllium-copper alloy strip for three and a half years developed sarcoid-like granulomata on her hands and forearms, which had been scratched by the metal strip. She was found to have a pulmonary granulomatosis clinically similar to delayed chemical pneumonitis due to beryllium.

The case fulfilled all the criteria for diagnosis of systemic berylliosis and, in particular, illustrated eczematous hypersensitivity to beryllium shown by positive patch tests, to high dilution of beryllium salts, and a delayed sarcoid reaction in the skin used for the patch tests.

My thanks are due to Dr. Marjorie Clifton, of the Department of Medicine, Sheffield University, who carried out the respiratory function tests; to Dr. P. L. Bidstrup, of the London Hospital, for the estimations of beryllium in the urine and skin; to Professor D. H. Collins for the pathological reports; to Dr. J. M. Barnes, of the Toxicology Research Station, for the histochemical examination of the skin sections; to Mr. R. Brook for the photographs; and, lastly, to the patient, who submitted most willingly to the lengthy investigations.

[A short report of this case has already been published in the *Proceedings of the Royal Society of Medicine*, 1955, **48**, 175.]

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Progress in the various branches of science needed for pest control is reviewed in the Pest Infestation Research Board report for 1954 (H.M.S.O., 3s.). The biology section is studying the population of pests associated with buildings, such as invest birds' nests or bat roosts; and also the populations found on stored materials, particularly those of the Khapra beetle—a serious pest in the maltings of Britain. The laboratory successfully fumigated Nelson's H.M.S. *Victory* with methyl bromide. No major change is reported in the work of the insecticide section, which has made considerable progress in studying the relative susceptibility of insects to insecticides. Paradichlorbenzene, in a test where Service uniforms were exposed to infestation for eight weeks, was found to kill all adult carpet beetles and 90% of the larvae; eggs hatched, but the young larvae died. 2% chlordane in refined kerosene painted in 3-in. (8-cm.) bands along the foot of walls, pipes, sinks, etc., and 5% chlordane in a non-inflammable oil on the outside walls, rid a 17-ward tuberculosis sanatorium of Pharaoh's ant at a cost of £75. Pit storage of grain is being tested throughout Africa and Cyprus; a gas-proof sheeting material is being tried out for this in collaboration with the Ministry of Supply.

GUILLOTINE TONSILLECTOMY AND CURETTAGE OF ADENOIDS UNDER ETHYL CHLORIDE ANAESTHESIA

BY

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This paper had been completed before the recent correspondence on the guillotine operation appeared in the *British Medical Journal*. This correspondence confirms our impression of the misunderstanding which exists concerning the guillotine operation and the anaesthesia required for it.

The published objections to the operation for removal of tonsils and adenoids in children by guillotine and curette under ethyl chloride anaesthesia would lead one to suppose that it was a thoroughly unsatisfactory procedure. This conclusion is entirely at variance with our experience; we here attempt to explain why this should be so, and why these objections should have gained such wide currency. In addition, we examine the suitability and safety of ethyl chloride as an anaesthetic agent for this operation.

Introduction

Removal of the tonsils is an extremely old operation, and is believed to have been practised before 53 B.C. It is, however, difficult to suppose that complete enucleation was often achieved, or that any definitive operation was possible before the introduction of anaesthetics. Nevertheless, in view of the technical difficulties (apart altogether from any considerations of humanity), it is worth noting that removal of the tonsils and adenoids in children entirely without anaesthesia has been not only practised but actually recommended, both in this country (Sydenham, 1935) and in Egypt (Shaheen, 1935), a mere twenty years ago.

Nowadays tonsillectomy is performed either by planned dissection or with the guillotine. Either method may be used in children, except in the presence of peritonsillar fibrosis, where, as in adults, dissection is by universal consent the correct procedure. Waugh (1909) drew attention to the poor standard of work being done with the guillotine, and recommended dissection. More recently Jobson (1942) gave what we believe to be the correct answer—namely, "... undoubtedly a great deal of bad work is done with the guillotine ... [but if] Sluder can produce 99.6% of complete enucleations, the method cannot be at fault." Throughout the intervening years the controversy over the respective merits of the two procedures has been bitter; but it is not our purpose to argue in favour of the superiority of one or other. We are concerned merely to record our impressions of what we regard as a satisfactory operation.

Technique

We have used the guillotine operation extensively in children up to the age of about 14 years, except, of course, in those with obvious peritonsillar fibrosis, and the details of the technique employed are as follows.

The only pre-operative medication administered is atropine sulphate, 1/100 gr. (0.65 mg.) injected subcutaneously about 45 minutes before operation. The gag is not inserted before beginning the induction of anaesthesia.

The child is "coaxed" to sleep with nitrous oxide from a Boyle's machine, while the anaesthetist simultaneously utters simple phrases of explanation and reassurance. The mask is applied to the face only when unconsciousness has supervened, and a little oxygen is then admitted. After a few further breaths the nitrous oxide is turned off, and some 5–10 ml. of ethyl chloride is introduced gradually into the breathing-tube. The anaesthetist indicates that the depth of anaesthesia is suitable by raising the child's head and shoulders, while a nurse removes the mask with one hand and places a small sandbag under the shoulders with the other. The surgeon now inserts the gag on the left side and opens the mouth. From this point on, the anaesthetist controls the gag with his left hand, and with his right he modifies the position of the head from moment to moment to suit the manœuvres of the surgeon.

The surgeon next introduces the guillotine and removes each tonsil in turn, the anterior faucial pillar being gently pushed off the tonsil by one or more partial closures of the blade before the guillotine is fully closed. Each fossa is then inspected and palpated. The adenoids are then removed, the curette being introduced as often as is necessary to achieve complete removal. The child is turned over on its right side, the throat is mopped out and reinspected and the gag is removed. The chin is pushed forward routinely lest, as sometimes occurs, the temporo-mandibular joints should have been subluxated.

The patient's face and neck are liberally sponged with cold water; and finally, when the protective reflexes have manifestly returned and the bleeding has abated, the child is carried back to the ward head down, and placed in bed in the lateral or semi-prone position.

Discussion

Certain aspects of this procedure merit some discussion.

1. Pre-anaesthetic Sedation.—We believe that the dangers (Jackson, 1951) of administering pre-operative sedatives to children have been exaggerated; and we are not opposed in principle to their rational use (Anderson, 1952) in order to achieve a carefully judged effect. However, children thus sedated may exhibit post-operative somnolence and later restlessness, demanding a degree of continuous individual attention for a variable period. We feel that the necessity for sedation can be virtually eliminated if the children are handled at all stages with a sensible mixture of tact and frankness, and if, above all, they are subjected to a considerate induction of anaesthesia.

2. Anaesthesia.—The considerate induction referred to is provided by nitrous oxide and oxygen, as described above, since we agree with Bromage (1950) that it is "... more acceptable to the apprehensive patient than the most humane ethyl chloride induction." The nitrous oxide/oxygen/ethyl chloride sequence has been described before in various forms by Westell (1941), Minnitt and Gillies (1948), and Bromage (1950), among others. We have found that the great majority of children accept it almost without a murmur, though the amount of encouragement and persuasion required varies considerably. A few are a little tearful, but if sufficient patience is exerted none need be terrified. This picture presents a happy contrast to scenes which many doctors must recollect with distaste. Though it may seem obvious, it is worth pointing out that the dose of ethyl chloride for any given child is that amount which is required to produce the desired level of anaesthesia. There is no standard dose, and it is wise to have available rather more than is thought will be necessary. There are three main grounds for advocating a pleasant induction:

(*a*) All creatures have the right to expect that unpleasant procedures to which they have to be subjected in their own interests shall be made as tolerable as possible. This applies with even greater force to children than to adults, in that the former are more vulnerable because of their immature level of understanding, and because they are of necessity less able to protest effectively against callous handling.

(*b*) Many authors—for example, Burstein (1953) and Capon (1954)—have called attention to the psychic trauma which may follow crude induction of anaesthesia in children. Jackson (1951) cites night terrors, temper-tantrums, destructiveness, and increased fears. Gorham (1935) wrote: "... children may change in character ... becoming nervous, irritable and waking up at night screaming ... in some cases these symptoms last a week or two, in others as long as nine months. Nocturnal sedatives have had to be administered for quite long periods." Deming (1952) believes that the normal emotional growth of children may be disturbed by fears, obsessions, and regressive behaviour resulting from unpleasant anaesthetic encounters.

(*c*) No doubt large numbers of normal well-balanced children who are subjected to disagreeable experiences escape actual psychic trauma, but it is evident that a persistent fear of hospitals and everything connected with them may result. The development of such an attitude, which at best prejudices adjustment to the crisis of illness and at worst endangers life itself—for example, in cancer (Aitken-Swan and Paterson, 1955)—must be countered by every possible measure.

As well as fulfilling the foregoing psychological criteria, the method described provides for the immediate and continuous availability of oxygen. The importance of avoiding anoxia in all circumstances, and particularly in the presence of a potentially toxic agent such as ethyl chloride, has been repeatedly stressed, and is now very widely appreciated (Bird, 1930; Bromage, 1950). It is disturbing to learn that the use of oxygen with ethyl chloride has been deprecated on the ground that it was responsible for a prolonged and turbulent induction (Kingsford, 1930).

3. *Use of Gag.*—The gag is inserted after the child is anaesthetized, because the conscious child dislikes the presence of a gag in the mouth—it is puzzling and frightening, and it hinders the accomplishment of a smooth induction. Also, it is often dislodged deliberately or inadvertently in early anaesthesia; and if not, teeth may be loosened or damaged if the jaws are clenched in the second stage. We have, in any case, never encountered any difficulty in introducing it after the required depth of anaesthesia has been attained. It is well known that spasm of the masseters may occasionally persist even in deep ethyl chloride anaesthesia. In this event, a combination of sustained downward pressure on the chin and counter-pressure on the forehead is employed to separate the teeth enough to permit insertion of the gag, which is then opened, assisted if necessary by the pressure of the surgeon's forefinger and thumb on the lower and upper incisors respectively.

4. *Inspection.*—Should the final inspection show, if ever, that a remnant has been left, anaesthesia is resumed with nitrous oxide, oxygen, and ether or trichlorethylene by insufflation through the side-tube of the Boyle–Davis gag, or (preferably) through a nasotracheal tube; and the surgeon then dissects out the remnant.

5. *Recovery.*—The use of cold water slightly accelerates recovery from the anaesthetic by reflexly stimulating the respiration. It is also thought to hasten the arrest of bleeding, probably by inducing reflex vasoconstriction.

Classical Objections Considered

The following selection is representative of the objections of the very numerous authors who have recorded their disapproval of the guillotine operation (the italics are ours throughout).

Sharp (1952) sums up thus: "The guillotine, in the hands of experts, usually results in a satisfactory removal of large pedunculated tonsils, but the buried fibrotic tonsils present difficulties, and removal of them results in damage to the pillars of the fauces; the *necessarily light anaesthesia* generally employed gives little time for a deliberate and considered removal of the adenoids." He also remarks that, while the dissection method is the more leisurely procedure and is the operation of choice, it must be undertaken with the co-operation of an *experienced anaesthetist*.

McKenzie (1951), discussing the question "Dissection or guillotine?" remarks that there are failures with both methods, but that poor results due to the guillotine are the more common. He goes on to give a graphic description of how they occur: "Most people are right-handed, and they seize the guillotine in their right hand, so that the right tonsil is removed first. The mouth now fills with blood, the patient may be *lightly anaesthetized* and cough repeatedly, and the left tonsil is hard to grasp. In consequence, a tonsil remnant is more likely on the left side." This is indeed a terrifying picture.

Atkinson (1942) is even more dramatic: "... hurried manipulations terminating in a rising tide of blood. ... The *lightly anaesthetized* patient is turned over, and, against a tightening barrier of resistant palatine muscle, the curette is forced into the nasopharynx. ... The adenoids become a concluding gesture in a welter of blood and confusion."

Laurence (1942) states: "... one should use an anaesthetic which permits one to do all that one wants to do." But he considers that ethyl chloride emphatically does not fulfil this specification.

Scott Stevenson (1952), comparing the two methods, considers that, though the dissection method possesses the greater advantages, it is not easy, takes longer, and requires a longer and *deeper anaesthesia*.

The criticisms embodied in these views may be grouped under two headings:

(1) That it is difficult to be certain of removing the tonsils completely, especially if they are buried or fibrotic; and that the faucial pillars and the palate may be damaged in the process. We have not found this to be so, but we have no doubt that if the guillotine is used routinely there will be failures attributable to peritonsillar fibrosis. From the description of our procedure it should be evident that there is ample *time* for the careful removal, inspection, and palpation mentioned. The other essential, if the peritonsillar tissues are to escape damage and easy access to the adenoids is to be provided, is that the musculature of the faucial pillars and soft palate be well *relaxed*—and this leads to the second group of objections.

(2) That the supposedly inevitable lightness of the anaesthesia, by providing inadequate muscular relaxation and compelling the surgeon to hurry, increases the hazards mentioned under (1) and impedes access to the adenoids. We are driven to conclude from the opinions previously quoted that the respective authors have based their views on the efforts of anaesthetists inexperienced in the use of ethyl chloride.

The guillotine operation is often regarded as a trivial one, and until quite recently the anaesthesia was commonly entrusted to the most junior member of the surgical team. He usually approached his task with reluctance and fear. The only positive element in his attitude was a vague but correct belief in the potency of the agent. Consequently it became his fixed resolve to brave the surgeon's annoyance at an inadequate anaesthesia rather than to run the slightest risk of the fatal result which he dreaded. Conversely, an occasional death may be attributable to a perverse determination in the opposite sense. Thus, we interpret the prevalent dislike of the guillotine operation as being largely an oblique protest against the inexpert anaesthetist.

It cannot be too strongly emphasized that, far from being light, the anaesthesia must, on the contrary, be *deep*—a little deeper initially than the average depth of the anaesthesia for the dissection operation. The coughing and swallowing reflexes must be suppressed and the pharyngeal and palatal musculature fully relaxed to permit deliberate surgery. Further, with an agent such as ethyl chloride, which is highly volatile, and rapid both in its action and in its elimination, the *duration* of anaesthesia is closely related to the *depth* attained by the time the mask is removed. Thus, apart from providing the necessary relaxation, a reasonably deep anaesthesia assists the surgeon by allowing him longer operating time.

Moreover, is expert anaesthesia so essential for the dissection operation? Certainly, the more experienced the anaesthetist the better—but sometimes a choice has to be made. If so, we believe that the more experienced anaesthetist should be allotted to the guillotine operation, and

the less experienced for the dissection. A competent E.N.T. surgeon can help a novice anaesthetist who gets into difficulties with an endotracheal tube; and if at any time during the operation the level of anaesthesia becomes too light he can stop and wait for a minute or two until the situation is corrected. Such delays may be irksome, but they do not jeopardize the essential success of the procedure. With the guillotine operation, however, the situation is reversed. The services of an expert anaesthetist can be used to imbue a trainee surgeon with confidence by allowing him to concentrate entirely on the surgical aspects and by safely providing adequate operating-time.

Estimates of the time required for guillotining the tonsils and curetting the adenoids, and also of the time which the single-dose administration of ethyl chloride provides for the operation, vary considerably. Thus, for the operation, times as short as 30 seconds (Shaheen, 1935) and 40 seconds (Newell, 1930) are declared to be ample. Bird (1930), on the other hand, estimated his average operating time at 115 seconds, and did not find this restricted by the anaesthetic technique. Others (Atkinson, 1942; Laurence, 1942) consider that ethyl chloride cannot be relied on to provide enough time for satisfactory surgery.

We find that the surgeon has an average time of about 90 seconds at his disposal, and that this is long enough for a trained operator to accomplish his task in comfort. If the surgeon so requests, the anaesthesia can be deepened more than usual before removing the mask, and the operating-time thereby safely increased to at least two minutes.

Dangers of Ethyl Chloride

Warning of the dangers of ethyl chloride are numerous. Thus, an authoritative textbook of pharmacology (Goodman and Gilman, 1941) states: "... although ethyl chloride is less toxic than chloroform, ventricular fibrillation and sudden cardiac arrest may occur." Stirling (1954) considers that atropine is essential to protect against primary cardiac failure due to vagal stimulation. Leigh and Belton (1946) recommend "adequate premedication" with atropine, but it is more than doubtful if their scheme of dosage fulfils their own criterion of "adequacy."

From recent experimental and clinical studies (Virtue and Pierce, 1951; Bush, Bittenbender, and Adriani, 1952) we conclude that, although these statements are probably applicable to the dog, they cannot be regarded as proved for human subjects. Even in light *chloroform* anaesthesia, the protective role of atropine is doubted (Clark, 1952).

It must be assumed that ethyl chloride has been commonly administered to patients who have not had atropine, or who have had it in theoretically inadequate dosage. Series of 40,000 (Sington, 1930), 30,000 (Hewer, 1930), and 11,723 (Kingsford, 1930) ethyl chloride anaesthesias without a fatality have been reported. None of these authors stated his views on the role of atropine, and we must therefore conclude that they did not employ it, or that they considered its contribution to safety insignificant.

Since, however, most surgeons regard a dry mouth as essential in tonsillectomy, there need be no further discussion of this point.

Various authors (Jobson, 1942; Macintosh and Bannister, 1947; Minnitt and Gillies, 1948; Deming, 1952) draw attention to the dangers and disadvantages of ethyl chloride, including its depressant effect on the myocardium, the narrow margin between the effective and the lethal dose, the liability of laryngospasm, post-operative vomiting, and liver damage, and its potency and the consequent risk of overdosage. In some schools these considerations have been taken so seriously as to lead to the abandonment of ethyl chloride. We have no doubt that this view is too extreme, but we do not enumerate the risks of ethyl chloride anaesthesia merely to dismiss them—rather to emphasize our point that it should be entrusted only to those who have become skilled in its use through proper training and supervision. With this qualification it has proved in our hands to be an admirable agent for the operation under discussion.

Mortality

During the ten-year period 1943–52 the operation of guillotine tonsillectomy and/or curettage of adenoids was performed on 12,038 children up to the age of 14 in Carlisle and the surrounding district by Mr. R. S. Venters or one of his registrars, without a single death.

The only other comparable series which has come to our notice is that of Martin (1922), embracing 14,960 cases operated on in a teaching hospital between 1907 and 1920 with six deaths. Minnitt and Gillies (1948) quote this series along with a personal communication from the author which brings the total number of cases to 23,960, and the deaths to eight. The series is not in fact strictly comparable to ours, because in a small number of cases (not stated exactly) the tonsils were dissected, and it was not wholly confined to children. Nevertheless, all eight deaths were in children undergoing the guillotine operation. In fairness we must state our belief that the contrast in the mortality between Martin's series and our own is largely due to the spectacular improvement in the health of the general population, and especially in that of the "hospital class," during the last two decades.

Summary and Conclusions

Guillotine tonsillectomy and curettage of adenoids carried out by an experienced surgeon, under ethyl chloride anaesthesia administered by a *competent anaesthetist*, is a satisfactory operation.

The procedure, as carried out by us, is described in some detail, emphasis being laid on the necessity for a considerate induction of anaesthesia.

Those who have recorded their objections to the operation base their opinions on an experience of inexpert anaesthesia, usually too light.

Contrary to widespread belief, the operation requires an anaesthesia of considerable depth.

The competent anaesthetist, who is aware of the dangers of ethyl chloride, can employ it safely.

A recent series of over 12,000 cases without a death is recorded, and contrasted with one of some 25,000 dating from the first quarter of the century, in which there were eight deaths.

We are indebted to Mr. R. S. Venters for making his records available to us and for his advice.

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ANXIETY REACTIONS IN HYPNOSIS

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Many patients exhibit some minor degree of anxiety when the question of hypnosis is first put to them. This is a fairly normal reaction. It is of little consequence, and is ordinarily minimized by establishing good rapport with the patient before mentioning the idea of treatment by hypnosis.

At the Threat of Loss of Ego Control

A mild, transitory anxiety reaction in the early stages of induction is very common. This is associated with the relinquishing of voluntary control. The abandonment of volition is a threat to the ego. It would seem that, under these circumstances, anxiety functions as a warning that all is not well with the psyche. For example, when hypnosis is being induced by suggestions of relaxation, it often happens that the first few suggestions are accepted easily; the patient relaxes, the limbs become flaccid, the facial muscles lose their tone, and the lips tend to gape. At this stage, when the patient is just on the verge of abandoning ego control in favour of the therapist, there is an exacerbation of anxiety. It is manifested by a general increase in tension. The relaxation is not so complete; the naso-labial folds become more marked; there may be some degree of furrowing of the brow and a slight tightening of the lips. If the anxiety is not recognized it may motivate the production of defences against hypnosis, particularly in the form of restlessness, which not only provides an outlet for the anxiety but also serves as an effective defence against hypnosis by relaxation. On the other hand, as soon as the anxiety shows itself the suggestions of relaxation can momentarily give way to suggestions of calm and ease and security. The patient becomes aware of the therapist's empathy; he is reassured; the affective relationship is intensified; and the anxiety is allayed.

This type of anxiety reaction occurs more frequently when rapport with the patient is inadequate. A satisfactory affective relationship with the patient prior to hypnosis makes it easier for him to introject the idealized figure of the therapist, and the abandonment of ego control becomes so much the smoother.

At the Sudden Awareness of Hypnosis

In other circumstances much more severe anxiety reactions may occur. Occasionally during the induction, patients experience a sudden violent paroxysm of anxiety. This is quite distinct from the mild anxiety described above. It occurs in patients who may have given verbal acquiescence to the idea of hypnosis, but who nevertheless really believed that they could not be hypnotized. The acute anxiety follows the patient's first awareness that he is in fact hypnotized and has lost voluntary control.

Some patients defend themselves against hypnosis by simulation. By consciously carrying out all the therapist's suggestions the patient feels that he obeys the suggestions voluntarily, and by so doing has avoided being hypnotized. Sometimes it is obvious that the defence is used in clear consciousness; at other times it would seem to be an unconscious mechanism. If the patient is allowed to persist with his defence he actually becomes hypnotized, but he is not aware of it until he is challenged. It is at this moment that acute anxiety may be precipitated. The reaction is accompanied by the physical signs of anxiety, pallor, tremor, sweating, dilatation of the pupils, and rapid shallow breathing. The pulse is rapid and may be thready or full and bounding. To this there may be added a certain degree of collapse. The suddenness with which the condition may develop can be quite alarming. The natural impulse to terminate hypnosis and wake the patient must be resisted. Suggestions of relaxation, drowsiness, and eventually sleep are added. Provided the patient is kept hypnotized this episode is easily managed, but there is a tendency for the acute anxiety to bring the patient out of hypnosis. The anxiety comes on without warning, and develops very quickly. Accordingly, it is wise to deepen hypnosis immediately the first signs of anxiety are observed. It is obviously very important that the therapist does not communicate to the patient his own anxiety by any non-verbal or extra-verbal means.

A company director in his late forties sought relief from tension and depression. Two years previously he had been treated with narcoanalysis and E.C.T. without improvement. He was a hysteroid personality, and fancied himself as an amateur actor. On a verbal level he desired hypnosis. His first defence was by depreciation. He depreciated the whole situation. By non-verbal means he conveyed the idea that the whole thing was silly. Induction was made by arm levitation. On the first suggestion of lightness of his hands he immediately lifted his arms into the air. When movement was suggested he straightway waved his arms about. He was smiling all the time, and it was obvious that he was defending himself by simulation. Following suggestions, various antics were performed with his arms, and he was allowed to believe that the therapist thought him hypnotized. He was in no way challenged, and was dismissed without comment. The same procedure was repeated in the second session, and in the third session the patient was suddenly challenged to put his arms down. He was unable to do so, and immediately developed an acute anxiety reaction. The anxiety was controlled by a deepening of hypnosis, and by allowing the patient to lie down. Subsequent hypnosis was uneventful.

At the Sudden Awareness of Repressed Material

A more common type of anxiety reaction occurs when a patient suddenly becomes aware of repressed traumatic material. Of course, this kind of reaction may occur in any type of reductive psychotherapy, but it occurs more readily in hypnoanalysis because the hypnotic state can allow the sudden surge into consciousness of repressed conflicts. In this respect it is important to distinguish between release of repressed material and awareness of the material. It would seem that, so long as the patient remains reasonably deeply hypnotized, the release of repressed material, by verbal ventilation, by acting out, or by projective techniques, does not produce anxiety. The hypnotized patient can express the traumatic conflicts in words, he can abreact and express the emotion appropriate to the conflict without producing anxiety; but if, for one reason or another, the hypnosis becomes lighter and the patient is able to comprehend in consciousness what he is expressing, then there may be a severe acute anxiety reaction. There is danger in the therapist becoming too interested in the content of the repressed conflicts and failing to keep watch on the depth of hypnosis. Abreaction itself may lighten hypnosis to such an extent that the patient may wake spontaneously, and in such circumstances acute anxiety may result.

There is another factor. Sometimes the production of anxiety from the sudden awareness of repressed conflicts is dependent on the means by which the repressed conflicts are expressed. In hypnoanalysis the conflicts are ordinarily expressed in words. Material that is too traumatic to be borne in consciousness is dealt with by the various psychic defence mechanisms and is again repressed, so that, on waking, the patient may remember the less traumatic incidents but has a spontaneous amnesia for the more traumatic material. But in hypnography—a technique in hypnoanalysis in which the hypnotized patient projects his conflicts by painting or drawing—these defence mechanisms cannot work so easily. The spoken word is transitory; it is easily repressed and forgotten. The painted representation of a conflict has a degree of permanence. The patient is confronted with it, and it tends to impress itself much more on his conscious awareness. Although the paintings are removed before the patient is awakened from hypnosis,

experience suggests that this type of acute anxiety reaction tends to occur more often during hypnography than in verbal hypnoanalysis.

An inadequate, dependent young man was receiving treatment for loss of confidence. When hypnotized he was given a crayon and told that his hand would draw something that represented his problems. With a rhythmical movement he made a series of marks on the paper. He became more and more preoccupied with what he was doing. The rhythmical character of the movement became more pronounced. His expression was very intense, and it seemed obvious that the drawing was a sexual equivalent. He began to verbalize his thoughts, and the sexual nature of the activity was confirmed. He abreacted a good deal of emotion. Hypnosis became lighter. He suddenly turned very pale and started to sweat. He woke from hypnosis spontaneously. In a shaky voice he said that he thought he had woken up and thought he was going to vomit. He became intensely tremulous; the sweating was profuse; his pulse was rapid and of poor volume. He looked alarmingly ill. He was immediately rehypnotized and given suggestions of calm and well-being. His physical condition was restored in ten to fifteen minutes. In subsequent sessions care was taken to maintain an adequate depth of hypnosis, and no further complications were encountered.

At the Inability to Fulfil a Post-Hypnotic Suggestion

Post-hypnotic suggestion is the spear-head of suggestive therapy, but this extremely useful weapon may at times be the means of precipitating an acute anxiety reaction. There is an extremely compelling quality about a post-hypnotic suggestion, and if the patient is unable to carry it out an acute anxiety reaction may result. In this respect it does not matter whether the patient is prevented from fulfilling the suggestion by reason of outside environmental factors or by reason of psychic factors within himself.

Accordingly, in suggestive therapy, specific post-hypnotic suggestions are best used sparingly and only when it is as certain as possible that the patient has both the material and the psychic means of carrying out the suggestions. On the other hand, non-specific post-hypnotic suggestion has not the same power to produce anxiety reactions, but nevertheless can give suitable patients considerable symptomatic relief.

A man of obsessive personality sought relief from particularly intractable insomnia of many years' duration. The severity of the insomnia had been confirmed by the hospital night staff, who reported that the patient hardly slept at all. He had previously been treated by narcoanalysis, "somnifaine," and E.C.T. without benefit. At different times he had been addicted to both paraldehyde and chloral hydrate. He also complained of irritability and uncontrollable rages. He was easily hypnotized, and after several sessions he was given the strong post-hypnotic suggestion that he would sleep each night without sedative until I saw him in a week's time. He was unable to fulfil the post-hypnotic suggestion, and arrived for the next appointment in a state of acute anxiety and covered with a generalized dermatitis. He was given suggestions of calm and relaxation, and ordered to take a sedative at night. In a week's time both the anxiety and the skin condition had subsided. He subsequently gained almost complete relief from the irritability and rages, although the insomnia persisted.

Discussion

Recent British and American literature suggests that there is a revival in the use of hypnosis, not only by psychiatrists using specialized hypnoanalytical techniques but also by the profession in general. Fortunately, acute anxiety reactions are not common, but when they do occur they may be alarming on account of the severity and the rapidity of onset. During the hypnotic session such reactions may occur from the sudden realization of having been hypnotized, or following the sudden awareness of repressed material. In each case the situation is met by immediately increasing the depth of hypnosis or by re-hypnotizing the patient. Hypnosis with suggestions of calm allows the usual psychic defence mechanisms to re-establish themselves, and material that is too traumatic at the present degree of insight is automatically repressed again. Any attempt to deal with this type of acute anxiety at a conscious level is likely to get out of hand, and is best avoided.

Anxiety reactions from the inability to fulfil a post-hypnotic suggestion usually occur in the absence of the therapist. Such reactions can be minimized by using non-specific post-hypnotic suggestion, where possible, in place of specific suggestion. Specific suggestion should be used only when it is reasonably sure that the patient has both the physical and the psychic ability to fulfil the suggestion.

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TRAUMATIC RUPTURE OF THE PANCREAS

BY

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Traumatic subcutaneous rupture of the pancreas is a relatively rare condition. It was first reported by Travers (1827), whose patient was crushed by the wheel of a coach. The subject was reviewed by Stern (1930). Phillips and Seybold (1948) noted that the diagnosis was made pre-operatively in only 4 out of 15 cases found in the literature of the previous ten years. The pancreas lies deeply in the abdomen and is normally well protected against possible injury. However, Aldis (1946) pointed out that if the abdominal muscles happen to be flaccid at the time of injury the pancreas may be crushed against the vertebrae, even by mild force. A variety of other mechanisms may cause pancreatic injury; in a case described by Keynes (1944) rupture was apparently due to blast from an under-sea explosion. As might be expected, injury to the pancreas is often accompanied by damage to other abdominal organs, as in Travers's case, when both duodenum and jejunum were involved. This often complicates early diagnosis but makes operative treatment imperative. The case reported below was one of complete rupture of the pancreas occurring as an isolated injury due to an apparently minor blow.

Case Report

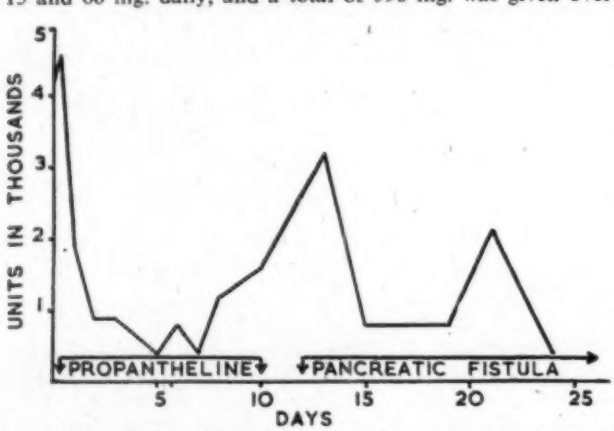
The patient was a young man, aged 20, in good health, with no previous medical history of note. About 24 hours before admission to hospital, while playing football, he had received a blow in the epigastrium from a player's knee. He felt "winded" and nauseated at the time. After a brief rest he returned to the field of play, but had to leave after a few minutes because he felt dizzy. He was able to go home after visiting the casualty department, where no serious symptoms or signs were found. Only slight epigastric pain was felt over the next few hours, but after a meal he vomited three times. The pain also became severe in the entire upper abdominal area. It was worse on moving and hiccuping. There was no pain in the shoulders or back. The pain and vomiting persisted during the night until his admission to hospital the following day.

When first seen he seemed in good general condition and had only moderate epigastric pain. The axillary temperature was 99.2° F. (37.3° C.), the blood pressure 120/80 mm. Hg, and the pulse 88. He was well coloured, the extremities were warm, and the veins were well filled. There was no wound or bruising of the abdominal wall. Only a minor degree of abdominal tenderness was present, generalized but more noticeable on the left side of the abdomen and in the left flank. No true rigidity was found, but there was some increase in muscle tone, again more pronounced on the left side. It was thought that a small amount of fluid was

present in the peritoneal cavity, as shifting dullness was elicited on the left side. Liver and spleen were not palpable. Bowel sounds were diminished, only an occasional sound being heard. Physical examination was otherwise negative. The urine was normal. Radiological examination of the abdomen showed slight gaseous distension of two loops of small intestine in the mid-abdominal region. During the next few hours an improvement occurred; the pulse remained between 70 and 80 and the temperature was 99° F. (37.2° C.). After drinking a cup of tea the symptoms returned; the pulse rose to 86 and the temperature to 101.6° F. (38.7° C.). There was a slight increase in abdominal tenderness and guarding. At this point, about 30 hours after injury, operation was carried out.

Under general anaesthesia, the abdomen was opened through a left paramedian incision. A mild peritonitis was present and a few ounces of blood was found in the left paracolic gutter and in the pelvis. A number of small white plaques were present in the mesentery of the proximal jejunum and in the retroperitoneal region, immediately to the left of the duodeno-jejunal flexure. Oedema and a dirty brown discoloration were seen in the lesser omentum and in the transverse mesocolon. On opening the lesser sac below the greater curvature of the stomach, the pancreas was found to have been completely transected from its upper to its lower border. This had occurred in the region of the portal vein and mesenteric vessels, so that the superior mesenteric artery could be seen pulsating, lying freely immediately behind the torn edge of the right segment of the pancreas. The two parts of the pancreas were separated by a distance varying from 1 to 2 cm. Very little blood was found in the neighbourhood of the injury and no active haemorrhage was occurring. The tail and distal part of the body of the pancreas were oedematous and felt hard and tense. The only other injury found was a small tear 5 cm. long on the costal surface of the right lobe of the liver involving little more than serosa. The abdomen was closed after leading a soft rubber drain to the site of rupture of the pancreas. No repair of the pancreas or pancreatic duct was attempted. The patient's condition at the end of operation was good, the blood pressure being 120/82 and the pulse rate 118.

Post-operative treatment was directed towards keeping pancreatic secretion at a minimum until healing of the pancreas had occurred, with a view to avoiding or minimizing pancreatic necrosis due to the liberation and activation of pancreatic enzymes. Little or no fluid was given by mouth for the first 48 hours after operation, and only 1.5 litres of intravenous fluid was given initially. Intravenous fluid therapy was then discontinued, as it was thought that the water administered might well increase the volume of fluid available for pancreatic secretion. In addition, propantheline bromide was given by mouth in a further effort to restrict the secretion of pancreatic juice. Dosage varied between 15 and 60 mg. daily, and a total of 390 mg. was given over the first 10 days. On one occasion, 24 hours after treatment, the drug was temporarily stopped, as the blood pressure had risen to 170/120. This rise did not recur when treatment with the drug was resumed.



Serial observations of serum amylase in a case of rupture of pancreas. Values in Somogyi units. The period of propantheline therapy and the delayed onset of pancreatic fistula are also shown.

The progress of the pancreatic lesion was followed by frequent estimation of the serum amylase. On admission, before operation, the level was 4,180 Somogyi units, rising to 4,600 units after operation. The series of estimations are shown in the Chart. Morphine was not used to control pain, because of its tendency to cause spasm of the sphincter of Oddi. Pethidine was found to be effective, but was required in a dosage of 300 mg. daily for the first three days. By the fifth post-operative day the pain had practically gone, but the patient was very restless. He found it increasingly difficult to swallow fluids and became extremely dehydrated. His weight fell to 6 st. 6 lb. (40.8 kg.) from a normal of 9 st. 11 lb. (62.1 kg.). On the following day the axillary temperature rose to 100° F. (37.8° C.) and a degree of peripheral circulatory failure was apparent; the blood pressure was 104/90 and the pulse rate 120, the extremities were cyanosed, and there was very poor filling of the skin vessels. Examination of the blood gave the following results:

Serum Na	340 mg. per 100 ml.
Serum K	22 " " " "
Serum chloride	620 " " " "
Co_2 combining power	46 vols. %

An intravenous infusion of dextran raised the blood pressure to 125/90, and water was given in the form of 5% glucose intravenously over the next 72 hours, by which time he was able to drink adequately and had made a striking clinical improvement. At the time rehydration was complete, coinciding with the end of propantheline therapy, a discharge of pancreatic fluid began from the drainage track. Little or none had occurred up to this point. Shortly after the fistula became active the serum amylase fell (see Chart). It had previously risen during the intravenous therapy. The clinical course now became uneventful, apart from a minor episode as shown by the last rise in serum amylase when the fistula became temporarily blocked. The fistula itself presented no difficulties in management, as only a small amount of pancreatic fluid was lost daily. The skin was prevented from digestion by aluminium paste. By the sixteenth day his weight had risen to 8 st. 8 lb. (54.4 kg.) and by the twenty-sixth day to 8 st. 11 lb. (55.8 kg.). The fistula healed and the patient was discharged after 33 days in hospital. When seen finally two months later, he was in excellent health and had no evidence of pancreatic dysfunction; his weight was static at his normal of 9 st. 11 lb. (62.1 kg.) and there was no radiological evidence of pancreatic calcification.

Discussion

Symptoms and physical signs following rupture of the pancreas can be very variable. They may occur early and be of a severity similar to those found in haemorrhagic pancreatic necrosis, or in others may be mild and delayed (Bockus, 1946).

Estimation of serum amylase may give valuable assistance in making the diagnosis, which should be suspected in all cases of upper abdominal injury. High values were found in all eight cases of a series described by Naffziger and McCorkle (1943). In the case described above, the amylase level seemed to follow the progress of the lesion with some fidelity. The treatment of the condition is operative, as otherwise it is impossible to decide with certainty what damage has been done to the pancreas or other organs. It would seem doubtful whether any operative repair of the pancreas should be attempted, as further pancreatic damage may be thus precipitated. It appears logical to attempt to cut down pancreatic secretion in the early stages to allow healing to occur. Both secretin and vagal mechanisms can be impaired to some extent by combining a reduction of oral intake with the use of a drug such as propantheline bromide. Care must be taken to avoid the production of a severe dehydration by this method.

Summary

A case of subcutaneous rupture of the pancreas due to an apparently minor injury is described. The treatment adopted was an exploratory operation followed by limitation of the secretion of pancreatic juice. The use of serial serum amylase estimations is recommended, both as a diagnostic test and as an index of the progress of the lesion.

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CHLORPROMAZINE HYDROCHLORIDE IN INTRAOCULAR SURGERY

BY

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Anaesthesia for intraocular surgery presents many special problems, and until recently it has not received serious attention from anaesthetists. Ophthalmologists have evolved a very efficient local analgesic technique, and operative results have on the whole been good, but there has always been the risk of an uncooperative patient. Furthermore, patients requiring intraocular surgery are frequently elderly, and the clinical picture is complicated by a varying degree of arteriosclerotic cerebral degeneration, so that complete co-operation cannot be assured. In addition, any operation on the eye must be an unpleasant experience for a conscious patient, who may flinch or "squeeze" the eye in such a manner as to jeopardize the ultimate result—a possibility which must be a constant source of anxiety to the surgeon.

Good visual acuity will often make a great difference to the mental and physical well-being of these difficult patients, so that any improvement in technique is important if it simplifies the surgeon's task and gives a better chance of success. Many patients requiring surgical intervention on the eye are suffering from general medical diseases—hypertension, cardiovascular disease, diabetes, chronic bronchitis—to say nothing of senility; and in this unit the pre- and post-operative supervision of the patient by the anaesthetist has proved of the utmost value.

Anaesthetic Requirements for Intraocular Surgery

The main anaesthetic requirements of a patient undergoing intraocular surgery are: (1) The anaesthetic technique must in no way raise the intraocular tension at any stage, and in fact should lower it so far as possible. (2) No sudden increase in arterial or venous blood pressure must be permitted, and when possible some degree of hypotension is desirable to lower the intraocular tension still further. (3) A tranquil recovery period free from restlessness, vomiting, coughing, and "squeezing" of the eye is essential; in fact a prolonged period of quiescence for at least 24 hours after the operation is an advantage and reduces the risk of ocular complications.

During the last few years we have endeavoured to improve the technique of anaesthesia for intraocular surgery. In the first place, a method was used whereby the patient was premedicated to such a degree as to produce almost light-plane general anaesthesia, and this was combined with local infiltration analgesia and general akinesia, using D-tubocurarine in sufficient doses to cause relaxation of the levator palpebrae muscle and paresis of the extraocular muscles. This method usually produced good results and eliminated the need for co-operation from the patient; it also overcame the hazard of "squeezing" of the eye during the operation and for some time afterwards, and furthermore it lowered the intraocular tension and thus reduced the chances of vitreous loss during extraction. The main difficulty was, however, to judge the patient's response to premedicant drugs. While in some cases the technique left little to be desired, in others the effect on the patient was such as to produce severe depression of the vital centres, particularly of respiration, so that the procedure became rather hazardous. Furthermore, some patients became excitable and unmanageable.

The Suitability of Chlorpromazine

Chlorpromazine hydrochloride ("largactil") has been used in anaesthesia as one constituent of the "lytic cocktail," a mixture of drugs calculated to depress tissue metabolism and inhibit compensatory autonomic reflexes, thereby reducing the amount of the agent required to induce and maintain anaesthesia; or it may be used to allow operation without a general anaesthetic at all, only local analgesia and a muscle relaxant being necessary. It has also been employed in psychiatric medicine for the treatment of conditions characterized by agitation and central psychomotor overactivity. It was on the last count that we thought that this substance might produce favourable circumstances for intraocular surgery and give more consistent results than the previous techniques.

Chlorpromazine hydrochloride has a variety of pharmacological actions; those important in intraocular surgery are: (1) production of sleep and general lowering of metabolic rate; (2) potentiation of the action of other analgesic and anaesthetic drugs; (3) depressant effect on the vomiting centres; (4) pronounced anti-adrenaline effect; and (5) some reduction in muscle tone. It has a prolonged action, during which the patient sleeps peacefully, returning gradually to full consciousness in 12 to 24 hours; further, although sleeping most of the time, the patient can be roused and answer questions rationally after one to three hours. There is a considerable degree of depression of cerebral activity, but, even so, the respiratory rate is not depressed as much as might be expected; actually the amplitude is slightly increased. The central depressive effect on the vomiting centre is particularly advantageous.

Its effect on the blood pressure in normotensive patients is not so marked, but the greater the degree of hypertension the more precipitous is the fall in blood pressure; however, in no case in the present series did a patient appear to suffer any ill effects as a result of this. There is often a preliminary rise in the pulse rate, but this soon settles at slightly above normal. The patient becomes pale, but the peripheral circulation appears good.

Technique

The night before operation patients receive sedation with quinalbarbitone ("seconal"), 1½ or 3 gr. (0.1 or 0.2 g.). One hour pre-operatively quinalbarbitone, 1½ gr. (0.1 g.) by mouth, and pethidine, 100 mg. intramuscularly, are administered; in some frail subjects the quinalbarbitone has been omitted. The patient is brought to the anaesthetic room 15 minutes before the operation is due to start. An intravenous injection of a mixture of 50 mg. chlorpromazine hydrochloride and 100 mg. pethidine diluted to 20 ml. with

sterile water is started. The injection is given slowly at the rate of about 1 ml. per minute until the patient falls asleep and can tolerate a lubricated artificial airway. The dose required varies from 20 to 45 mg. of chlorpromazine and 40 to 90 mg. of pethidine. During induction a few patients complain of thirst or palpitations, but these are of short duration. Patients even at this stage are often just capable of responding to shouted instructions, but in a most apathetic way, and their efforts are poorly maintained. On questioning afterwards they have no recollection of this; on the other hand, there appears to be no retrograde amnesia, and all remember coming to the anaesthetic room.

A regional infiltration with procaine is given, coupled with a retrobulbar injection. A long, narrow-bore tube connected to an oxygen cylinder is placed beneath the face towel so that the open end is in close proximity to the artificial airway in an attempt to keep the air circulating beneath the towels and increase the oxygen concentration.

The patient sleeps peacefully throughout the operation, and the operator can take as long as he wishes without the fear of a restless patient. After the operation patients cause the minimal amount of trouble in the ward, and the method has been well received by the ward sister. After one to two hours patients will often remove their own airways. Unless disturbed, they sleep for the remainder of the 24 hours. If roused they answer questions with progressively more enthusiasm, and quickly drop off to sleep again. Next morning they have all appeared normal, the majority having no recollection of the previous 24 hours.

Results

Since March, 1954, 80 patients have been anaesthetized in this way. Their ages ranged from 18 to over 80 years, the majority being between 60 and 80 years. Three-quarters of this number were undergoing cataract operations, and the remainder operations for glaucoma and corneal grafting. There has been no mortality or morbidity in this series, and the patients' post-operative condition has been excellent. Although the method has not been used on the extremely frail and those with severe cardiac disease, it has been used for nervous patients, and also in many cases with marked signs of arteriosclerotic cerebral degeneration where a purely local technique would have been dangerous.

In one case vomiting occurred four hours after the operation, but it was of very short duration, and in this case there was a history of many years' "gastric trouble." With this exception there has been no coughing or straining in the post-operative period and recovery has been extremely quiet and uneventful. Two cases of severe hypertension, both with a pre-operative systolic blood pressure of over 250 mm. Hg, caused some anxiety in the post-operative period. Soon after injection of the chlorpromazine–pethidine mixture the systolic blood pressure in both cases fell to between 70 and 90 mm. Hg, and it remained at this level for just over three hours post-operatively. Apart from the hypotension, the physical state of these two patients appeared satisfactory and the pulse remained slow and easily palpable. At the end of three hours the blood pressure began to rise slowly in each case, and returned to the pre-operative level in 12 hours. Both patients made an uneventful recovery.

Summary

A method of anaesthesia for use in intraocular surgery has been described, the agent being a mixture of chlorpromazine hydrochloride and pethidine.

The results obtained in 80 cases have been briefly recounted.

The main advantages of the method are: (1) no co-operation is required from the patient during the operation or for several hours afterwards; (2) it produces a low-tension eye ideal for intraocular surgery; and (3) the recovery period is extremely tranquil.

LIVER DAMAGE AND EOSINOPHILIA FOLLOWING CHLORPROMAZINE THERAPY

REPORT OF A CASE

BY

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A relationship between chlorpromazine therapy and liver damage has been recognized. The extent of liver damage varies; at least one fatal case has been reported (Boardman, 1954). Lemire and Mitchell (1954) mention the occurrence of transient eosinophilia during chlorpromazine jaundice. The present case report also illustrates this unusual phenomenon.

Case History

The patient, a man aged 52, was of Jewish extraction. During the last four years, electric convulsion therapy had been given elsewhere on some 30 occasions for a recurring depressive state. Between March 31 and April 12, 1954, chlorpromazine was administered orally, the total dosage being 1.5 g. His previous medical history and family history were not relevant. About ten days after beginning this treatment he became nauseated. During the next three days he became febrile and began to vomit. He complained of pain in all his joints, frontal headaches, rigors, loss of appetite, and colicky abdominal pain; he developed a continuous burning pain in the epigastrium. Chlorpromazine was suspended. Admission was arranged to the Royal North Shore Hospital of Sydney on April 19.

Physical examination revealed a well-developed middle-aged man who was obviously jaundiced. His temperature was 102.2° F. (39° C.). The liver was not palpable, but there was generalized abdominal tenderness, maximal in the right hypochondrium. There were no splenomegaly, no glandular enlargement, and no abnormality on rectal examination. The blood pressure at the time of admission was 75/50. Subsequent readings were in the order of 100/70. The urine was very dark, and analysis revealed the presence of bile pigments, bile salts, and an excess of urobilinogen. The first faecal specimen examined after admission was pale.

On April 19 the leucocytes numbered 15,300 per c.mm., of which 49% were eosinophils. On the 20th the white cells totalled 14,900 per c.mm. (eosinophils 58%); the serum proteins were 7.9 g.%, the albumin–globulin ratio was 2.4:1; the thymol turbidity was 1 unit (normal range 0–4); the serum alkaline phosphatase was 12.8 modified Bodansky units (normal range 2.2–8.6) (Shinowara *et al.*, 1942); and the serum bilirubin was 3.8 mg. per 100 ml. The Casoni test was negative, and no ova, cysts, or parasites were found in the stools. The chest *x*-ray findings were normal; the plain *x*-ray film of the abdomen showed no gross abnormality; repeated examinations of the stools for occult blood were negative; and the Eagle flocculation test was negative. Three days after admission the temperature had fallen to normal. A slight subjective improvement had occurred but he remained deeply jaundiced.

By April 30 the diagnosis had not been established, so it was decided to perform liver biopsy by needle aspiration. This was done on May 3. The section showed bile pigment in the bile canaliculi, mainly near the centres of the lobules. There was no accumulation of bile in the bile ducts of the portal tracts. The liver cells appeared healthy throughout. Some of those near the centres of the lobules had bile in their cytoplasm. In the supporting tissue of the

portal tracts there were more lymphocytes and histiocytes than normal. The fibrous tissue was not increased. The Kupffer cells contained no bile pigment. A diagnosis of biliary obstruction was made.

Laparotomy was performed on May 10. The gall-bladder was normal and the common duct was not dilated. On opening the duct there was only a moderate flow of bile. A probe was passed towards the porta hepatis. However, neither the right nor the left intrahepatic duct could be entered, and it was thought that there was an obstruction at the origin of the intrahepatic portion of the common duct. The common bile duct was drained, using a T-tube. No abnormality was found on palpation of the other intra-abdominal organs.

Apart from a low-grade post-operative fever, due to a pulmonary infection, and mild colicky abdominal pain, convalescence was uneventful. The quantity of bile which drained ranged from 75 to 480 ml. daily from the first to the tenth post-operative days. These figures are within normal limits (Rundle *et al.*, 1955).

Nine days after operation (May 19) a cholangiogram was done. The gall-bladder and bile ducts filled well and appeared normal. The biliary drainage tubes were removed on May 26. At this time the degree of jaundice was lessening (serum bilirubin 3.8 mg. per 100 ml.) and the patient was beginning to regain his appetite and to feel well. The eosinophils had fallen to 5% of 16,300 cells.

Improvement was steadily maintained, and when discharged on June 12 the jaundice had almost completely subsided and the patient was feeling well.

When last seen, on December 23, he appeared to be perfectly well; in the interim further shock treatment had been given. The serum bilirubin, the serum proteins, and the thymol turbidity values were normal, but the urinary urobilinogen was still increased. The total white cell count was 10,950 per c.mm., and 6% of these were eosinophils.

Discussion

Both the patient and his wife were convinced at the time of admission that the illness had resulted from chlorpromazine, and his medical attendants at first thought that he was suffering from hepatitis. It was necessary to distinguish between an obstructive jaundice and a hepatocellular jaundice. In favour of the former were the presence of dark urine containing bile pigments and salts, the pallor of the stools, and the rising level of the serum alkaline phosphatase. However, it was difficult to explain the presence of excess urobilinogen in the urine if this really was an obstructive lesion.

The presence of eosinophilia suggested the possibility of an allergic process. Hodgkin's disease was considered, but there were no enlarged glands and the spleen was not enlarged. Parasitic causes of eosinophilia were sought but were not found.

The results of the liver biopsy suggested an obstructive lesion, but this could not be definitely demonstrated at operation. In fact, the post-operative cholangiogram showed the biliary tree to be normal. A careful review of sections of the liver biopsy has since been made and the appearances are now considered to be those described in the so-called cholangiolitic hepatitis (Watson and Hoffbauer, 1946; Goulston and Smith, 1951).

It would appear, therefore, that this patient was suffering from a form of hepatitis. The biochemical investigations may be explained on the basis of hepatitis with obstruction.

Infective hepatitis must be considered in the differential diagnosis, especially as it is common in the Sydney community at present. Eosinophilia does not appear to have been reported in this disease. On the contrary, it is stated (MacCallum *et al.*, 1951) that eosinophils are commonly absent in infective hepatitis. In this case the total number of eosinophils increased, attaining the high percentage of 58 at the height of the illness.

It is interesting that Lehmann and Hanrahan (1954) have noticed the occurrence of allergic reactions, such as urticaria and asthma. In their series of 71 patients treated over a period of four months with chlorpromazine, 13% showed such reactions. However, they do not mention eosinophilia. In our patient the eosinophilia may have been indicative of an underlying allergic reaction.

Lemire and Mitchell (1954) observed three cases of chlorpromazine jaundice in elderly people. In two of these patients a transient eosinophilia of 7 to 17% was noted. The liver-function tests revealed a hyperbilirubinaemia, an increased serum alkaline phosphatase, and a normal thymol turbidity. Two had liver biopsies performed, and all three were subjected to surgery. The authors consider that their patients were suffering from toxic hepatitis due to chlorpromazine, the mechanism of the complication being unknown. Their findings and conclusions correspond with our own.

Further observations will be necessary to establish whether our patient has sustained permanent liver damage as a result of chlorpromazine therapy. The presence of excess urobilinogen in the urine six months after apparent recovery does suggest this.

Summary

A case of hepatitis following chlorpromazine therapy is reported.

The occurrence of eosinophilia in this illness is discussed.

I wish to thank the General Medical Superintendent of the Royal North Shore Hospital of Sydney for permission to report this case; and Dr. F. A. E. Lawes, Mr. F. F. Rundle, Dr. I. D. Thomas, and Dr. K. Viner Smith for assistance in preparation of the paper.

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Medical Memoranda

Anaesthesia Following Long-term Oral Chlorpromazine Hydrochloride Therapy

A review by Dundee (1954) of the pharmacology and applications of chlorpromazine hydrochloride records the widespread clinical uses of this drug outside hospital practice, and the increasing possibilities of anaesthetists meeting emergency admissions so treated. The following case is put on record so that others may avoid "anaesthetist's distress" in similar cases.

Case Report

A feeble-minded man of 20, weight 11¼ stone (73 kg.), was admitted in February, 1955, with a diagnosis of acute appendicitis. He was given ¼ gr. (22 mg.) of "omnopon" and 1/150 gr. (0.43 mg.) of scopolamine one hour before operation, and was induced with thiopentone sodium 600 mg., and maintained with gallamine triethiodide, 100 mg., nitrous oxide and oxygen, and ether. There was a delayed return of normal respiration for three-quarters of an hour.

At operation a gangrenous retrocaecal appendix was removed. The operation lasted for one hour and he did not regain consciousness for the next four and a half hours,

tolerating an oro-tracheal airway during this period, the tube being necessary to prevent a valvular obstruction of his larynx by a mobile epiglottis.

His post-operation pulse rate rose to between 130 and 140 for the subsequent two days. There was no post-anaesthetic vomiting and he made an uninterrupted recovery.

COMMENT

The significance of the fact that this patient had been treated with oral chlorpromazine, 25 mg. three times a day, for the fourteen months previous to his admission was not appreciated at the time, and consequently he was given a normal anaesthetic for his age and weight, with the somewhat anaesthetically distressing results. The post-operation tachycardia and absence of vomiting are a well-known feature of chlorpromazine premedication. This case suggests that care should be exercised in giving normal doses of anaesthetic drugs to patients taking chlorpromazine.

My thanks are due to Dr. H. M. Bird for permission to publish this case.

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Prolonged Coma in Simmonds's Disease

Patients with Simmonds's disease often die in coma, which may be induced by various factors, such as the following.

Hypoglycaemia.—A low fasting blood sugar, sensitivity to insulin, and repeated hypoglycaemic attacks are often features of Simmonds's disease (Sheehan and Summers, 1949, 1952; Alexander, 1953). While in mild cases recovery may be spontaneous or may follow administration of glucose, prolonged hypoglycaemia may result in damage to cerebral tissue which is irreversible and fails to respond to glucose. Although the length of hypoglycaemic coma which prevents a full degree of physical and mental recovery must vary from case to case, Lawrence *et al.* (1942) suggest that "coma of one to three hours is usually associated with complete recovery, while longer periods are dangerous." Convulsions in hypoglycaemia have been mentioned as an important factor in preventing recovery from that state (Grayzel, 1934).

Hypothermia.—The profound lowering of the body's metabolic rate that occurs both in Simmonds's disease and in myxoedema may lead to a reduction of temperature sufficient to promote coma. Sheehan and Summers (1952) have shown that in a patient in coma with a very low temperature rapid recovery took place following immersion in a hot bath.

Low Blood Pressure and Loss of Electrolytes.—The adrenals are commonly atrophied in Simmonds's disease, and in some cases coma may be ushered in by marked hypotension and salt depletion, suggesting Addisonian crisis (Sheehan and Summers, 1949; Wolff, 1950).

The case here described makes it apparent that deep coma of 40 hours' duration, associated with hypoglycaemia and convulsions, can be followed by full mental and physical recovery.

CASE REPORT

A woman of 41, who had been unconscious with convulsions since about 1 a.m., was admitted at 2.30 p.m. on June 22, 1953. She was lying deeply comatose, slightly sweating, and with shallow respirations, in a pool of her own excreta. Her limbs were spastic, her trunk in opisthotonos, while every few minutes she was seized with generalized clonic and tonic convulsions associated with coarse grunting noises. Her temperature was 101.6° F. (38.7° C.), pulse 88, B.P. 120/70. Plantar reflexes were extensor, corneal reflexes absent.

The patient was moderately well nourished, with pendulous breasts; her skin was waxy pale, axillary hair was absent, and pubic very scanty. Following 50 g. of glucose intravenously, the convulsions became less severe, and on receipt of the blood-sugar report as 32 mg. per 100 ml. half an hour later, a further 100 mg. of glucose was administered intravenously with 100 mg. of cortisone acetate and 1 mega unit of penicillin intramuscularly. An intravenous 5% glucose-saline drip was set up. By 6 p.m. the blood sugar had risen to 86 mg. per 100 ml. and, although severe convulsions had ceased, she remained in deep coma, with extensor plantar reflexes. Cortisone, 100 mg. eight-hourly, was continued.

The next morning she was still deeply unconscious, and was incontinent of urine and faeces. The blood sugar was 140 mg. per 100 ml. During the day there were signs of improvement, and by 5 p.m. she had begun to stir and open her eyes. This was 40 hours after the known onset and 26 hours after the institution of treatment, during which she had been given 400 mg. of cortisone intramuscularly and about 260 g. of glucose intravenously.

From then on, progress was uneventful. On a regime of cortisone, 50 mg. daily by mouth, thyroid, 1 gr. (65 mg.), and methyltestosterone, 15 mg., she asserted she had "never felt better."

The electrocardiogram on admission showed low-voltage and flat T waves, later reverting to normal. The electroencephalogram after recovery showed no convulsive organic abnormality.

The history, obtained subsequently, revealed that the patient had had three children, there having been serious post-partum haemorrhage after the last confinement 16 years previously, and subsequent total amenorrhoea. Simmonds's disease was diagnosed elsewhere in November, 1952, and she had been on testosterone and thyroid since then. She had never had fits, but had had one previous short coma, without convulsions, in January, 1953.

COMMENT

Of the known factors which can induce coma in Simmonds's disease, hypothermia and Addisonian crisis can be excluded in this patient, and the question then arises to what extent the hypoglycaemia was responsible for the prolonged coma. In fact, during the latter 24 hours of coma the blood-sugar levels were within normal range, but, as is known in insulin overdosage, the return of the blood sugar to normal may prevent neither permanent mental damage nor a fatal outcome. We have been unable to find a case recorded in which full recovery occurred after hypoglycaemia so deep and prolonged, and it is possible that in our case other factors were partly responsible for maintaining the comatose state.

While cortisone plays an important part in the maintenance therapy of Simmonds's disease, treatment of the coma with cortisone has not been universally successful. Thus Sheehan and Summers (1952) found that intravenous cortisone produced no appreciable effect in two cases of hypopituitary coma, although it is not clear to what extent hypoglycaemia was a factor in those cases. We feel that administration of cortisone as well as glucose to our patient was largely responsible for the successful outcome. Cortisone has been used to combat hypoglycaemia of various causes, such as pancreatic islet tumour and Addison's disease, and we feel encouraged to use it in prolonged hypoglycaemia of whatever aetiology.

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Reviews

BRITISH SURGICAL PROGRESS

British Surgical Practice: Surgical Progress, 1954. Under the general editorship of Sir Ernest Rock Carling, LL.D., F.R.C.S., F.R.C.P., F.F.R., and Sir James Paterson Ross, K.C.V.O., M.S., F.R.C.S. (Pp. 348+vii; illustrated. 42s.) London: Butterworth and Co., Ltd. 1955.

This is essentially a continuation of the great work on *British Surgical Practice* edited by the same authors and brings that work up to date. It consists of three sections: original articles, critical surveys, and abstracts. They are all of a very high order, and either describe or provide access to the latest achievements of surgery.

The first article, by Rodney Maingot, is perhaps the most arresting. He describes in detail the injuries which may occur to the bile ducts and the results which may follow, often unfortunately as the result of surgical procedures. He explains how such mistakes may arise, and how they might have been prevented by a more accurate knowledge of the abnormalities which may occur and by more accurate technique. There follows an admirable account of the methods which have been evolved for the repair of such injuries, sometimes the most difficult problem with which a surgeon can be faced.

The article by Poole-Wilson on injuries of the urethra and bladder, fortunately of less common occurrence, is clear and the result of wide experience. It will be welcomed by all who have to deal with these difficult conditions. That by Paul Brand, of Vellore, on reconstruction of the hand in leprosy, is of far wider appeal than to his own special field, and all who have to deal with the restoration of the functions of the hand after nerve injuries will appreciate the value of his work.

Pelvic viscerectomy for advanced cancer is the subject of an article by Sir Stanford Cade, and is an example of the extraordinary lengths to which modern surgery can go. Such operations can, of course, be justified only in desperate cases and when undertaken by surgeons of quite exceptional skill and wide experience. But he shows that with these conditions they are fully justified and may give relief which can be obtained in no other way.

The article by G. A. Hay and F. W. Spiers on the application of electronics to clinical practice shows how dependent the surgeon of the future may be on physical science. One only hopes that it will be his servant and not his master. After all, one can use a microscope quite effectively without knowing anything about spherical aberration.

The critical surveys include several articles of value. Those on antibiotics and on blood transfusion show important progress in these fields. On carcinoma of the oesophagus Ross Robertson gives a full and well-illustrated account of what can be done with the resources of modern surgery. That many surgeons now question whether such operations are worth while in no way detracts from the value of the article. Norman Tanner gives an excellent account of the present position of carcinoma of the stomach and the encouraging results of modern technique. The abstracts furnish a brief account of progress in a large number of fields and afford ready access to the literature for those who desire to explore these subjects further.

We would like to congratulate the editors on the high level of material, and the publishers on the standard of production maintained throughout the volume.

HENRY SOUTTAR.

THE AUTONOMIC NERVOUS SYSTEM

Clinical Aspects of the Autonomic Nervous System. By L. A. Gillilan, Ph.D., M.D. (Pp. 316+xii; illustrated. 45s.) London: J. and A. Churchill, Ltd. 1955.

The intention of the author, who is associate professor of anatomy at the Graduate School of Medicine, University of Pennsylvania, is to assemble the facts known about the autonomic nervous system and "arrange them in such a way that the clinician will be able to use them in his practice." Unfortunately he has not been very successful in his task; there is a clear account of the anatomy and elementary physiology, but the clinical aspects are dealt with much less satisfactorily and there are some inaccuracies. The common accompaniment of narcolepsy is cataplexy with sudden loss of muscle tone, and not, as the author says, catalepsy "with statuesque attitudes"; while it has often been demonstrated that the common lesion of the posterior inferior cerebellar artery is a thrombosis and not, as the author implies, a haemorrhage.

There is a fairly comprehensive account of the mechanism of visceral pain, but no satisfactory description or explanation of the curiously localized shoulder-tip pain of subphrenic disease.

The bibliography is adequate, but it is strange to read in the preface that the autonomic nervous system got its first firm footing in medicine in 1935 when Max Peet devised his operation for the relief of hypertension; Leriche for a number of years before this had drawn attention to the clinical importance of the sympathetic nervous system, and in 1934 Gask and Ross had published a monograph on its surgery.

J. W. ALDREN TURNER.

GRENZ-RAY THERAPY

Grenz Ray Therapy: Principles, Methods, Clinical Applications. By Gustav Bucky, M.D., and Frank C. Combes, M.D. (Pp. 204; illustrated. 60s.) New York: Springer Publishing Company Inc. London: Lange, Maxwell and Springer, Ltd. 1954.

Grenz-ray therapy is not much used in this country, but it might be applied with advantage to patients suffering from superficial lesions of the skin and accessible mucous membranes and of the eye. The great difference between this form of treatment and that by more conventional methods of irradiation lies in the fact that, even with relatively large doses, so little penetrates to the deeper layers that the damage to the subepithelial connective tissues—for example, the dermis—is very slight. Thus, a dose to the epidermis of 1,000 r will deliver to the vessels of the dermis at a depth of 2 mm. only about 10 r, so that chronic changes due to vascular damage will be slight or non-existent. On the other hand, the doses delivered to these vessels even by so-called contact *x* rays for the same surface dose of 1,000 r will be of the order of 500 r—a dose by no means negligible, and capable, as any radiotherapist knows, of permanent irreversible damage to the vessels.

This, in essence, is the burden of the first part of this book concerned with physical and biological principles. The measurement of dose is not very thoroughly considered, but the absorption curves in tissues, carbon, water, and aluminium are thoroughly discussed, and the effect of air absorption on the beam and of oblique entry of the radiation into the tissues is stressed. These are considerations of little moment in most conventional *x*-ray treatment; indeed, the chief rivals to grenz rays in their particular field are likely to be artificially produced radio-isotopes, which have their limitations in convenience of application, especially to large areas.

The authors give a long list of successfully treated clinical conditions, especially of the skin. The chief advantage of grenz rays is the safety of repeating treatment to such lesions, even with much higher surface doses than would be safe with more penetrating radiation.

Since beryllium window tubes are now readily available and of constant performance this book should be in demand as a guide to all who begin to acquire experience in this field. It is well produced, and, although somewhat diffuse and repetitive, gives the answers to most of the questions likely to occur to those undertaking grenz-ray therapy.

FRANK ELLIS.

BIOLOGICAL SCIENCE

The Human Machine: Biological Science for the Armed Services. By Charles W. Shilling. (Pp. 292+xii; illustrated. $5.) Annapolis, Maryland: Naval Institute. 1955.

This book is primarily addressed to members of the United States Armed Forces, but much of its content will appeal to a wider audience. It is an expression of a view which is beginning to gain wide acceptance, particularly on the other side of the Atlantic—namely, that some general knowledge of human biology is of value to the ordinary man in his personal life and everyday work.

Part I is an orthodox elementary account of the structure and functions of the body, with some interesting observations on the potentials of human performance. Part II gives a reasonable and not too austere prescription for a healthy life. The reviewer would have been inclined to omit Chapter 9 altogether. It amounts to little more than a nominal list of diseases—a gloomy catalogue of disaster which does little to advance the book's general argument. The sections on first aid and emergency treatment follow generally accepted lines. It is noted with regret, however, that on page 31 the use of oxygen and carbon dioxide breathing mixtures is still advocated.

The third part will probably be new to many British readers and is the most interesting one in the book. Entitled "The Human Machine as Part of the War Machine," it deals with man in relation to the various special environments created by war and military equipment. It will probably engender in the non-medical reader a clearer appreciation of the importance of welding man, equipment, and operation into a single harmonious design. This is a lesson which has not yet been fully learned in all quarters.

The production and printing are of a high standard, though some of the diagrams will tax the presbyopic. Only one minor misprint was noticed.

J. M. HOLFORD.

VITAMINS

Vitamins in Theory and Practice. By Leslie J. Harris, Sc.D., D.Sc., Ph.D., F.R.I.C. Fourth edition. (Pp. 366+xxii; illustrated. 35s.) Cambridge: University Press. 1955.

It is a pleasure to welcome once more a new edition of this book, the previous edition having appeared as long ago as 1938. Many notable contributions to our knowledge of the vitamins have, of course, been made in the intervening period, but the text has been revised and brought up to date wherever necessary, and new chapters have been introduced to deal with some of the more important additions to our knowledge of the subject.

It is as well to point out, in view of the long interval which has elapsed since the notices of the previous edition appeared, that this account of the vitamins can be read with pleasure and profit by the "ordinary" reader, as well as by medical students, doctors, dietitians, and others with a professional background of interest in nutrition. The book is profusely illustrated and thoroughly deserves the continuation of the support it has received in the past.

S. J. COWELL.

POTASSIUM METABOLISM

Potassium Metabolism in Health and Disease. By Howard L. Holley, M.D., and Warner W. Carlson, Ph.D. (Pp. 131+xii; illustrated. $4.50.) New York and London: Grune and Stratton. 1955.

This book provides a concise and readable summary of current information on normal and abnormal potassium metabolism. The two authors write from the Departments of Medicine and of Biochemistry in the University of Alabama, and their collaboration has given us an exceptionally lucid account of the ways in which potassium metabolism influences and is influenced by energy metabolism. The part played by potassium in nerve and muscle activity is also outlined. Some exception may be taken to the authors' belief, implicit on page 17 and explicit on page 22, that "transfer of potassium between the intracellular and extracellular compartments is a relatively slow process"; for isotope studies, both *in vitro* and *in vivo*, indicate that transfer of potassium across the cell wall takes place very rapidly indeed.

The various clinical causes of potassium depletion and excess are adequately summarized; overdosage with deoxycortone acetate is mentioned, but aldosterone is referred to by its "old" name of electrocortin, and Conn's new syndrome of primary aldosteronism has not been anticipated. There is an appendix giving the potassium content of foods, and even of the public water-supply in 150 American cities; from this it would appear that only in Aberdeen, S. Dak., Galesburg, Ill., and Kansas City, Mo., could anyone expect to get as much as 1 mEq of potassium daily from the tap. This evidence of painstaking preoccupation with the needs of American readers may console any British kaliologist who happens to notice that in a list of 41 references it has not been found necessary to include any British work more recent than that of Sidney Ringer in 1883.

D. A. K. BLACK.

MARRIAGE GUIDANCE

Your Marriage: A Book for the Married and the About to be Married. By Kenneth Walker, F.R.C.S. Foreword by F. A. E. Crew, F.R.C.P., F.R.S., and a psychological postscript by Peter Fletcher. Second edition. (Pp. 150+xvi. 8s. 6d.) London: For British Social Biology Council by Secker and Warburg. 1955.

Any Wife or Any Husband: A Book for Couples who have met Sexual Difficulties and for Doctors. By Medica (Dr. Joan Graham). Second edition. (Pp. 147. 10s.) London: William Heinemann, Ltd. 1955.

These books were first published within a few months of each other, and it is remarkable that their second editions appear almost simultaneously. For they have no obvious connexion except their subject, and even to this they bring a different approach.

Mr. Walker's book has changed its title from *Marriage*, the possessive adjective being added to give it a more personal appeal. A psychological postscript also appears for the first time and discusses the role of emotional independence of the partners, and of social and economic factors, in determining stability of marriage. Otherwise the book consists of a simple short account of sex, adolescence and its problems, the choice of a marriage partner, the consummation of marriage, coital technique, the having and the avoiding of children, and mothers-in-law and other threats to domestic bliss. All will regard Mr. Walker's views on premarital chastity as realistic and honest, but some may find them unnecessary, at any rate in this context. The subtitle of this work, "A book for the married and the about to be married," is important in that it indicates its scope and also that it is intended for lay readers.

Medica's subtitle is equally important and revealing and reads, "A book for couples who have met sexual difficulties and for doctors"—a phrase which intrigues by its several possible interpretations. Difficult though her task may appear, there is no doubt that the author, a grandmother herself, has written something which should prove of the greatest help to the general practitioner and gynaecologist, and yet it is sufficiently non-technical to hand on to patients of average intelligence for their profit. It does not anticipate trouble, but has something practical to say to those who have tried and failed. It describes and comments usefully on the common disorders of sex encountered by both men and women: impotence, frigidity, lack of orgasm, dyspareunia, homosexuality, and various forms of maladjustment. Moreover, it answers reassuringly the many doubts and fears which a host of patients have always had but which they are more likely to ventilate to the doctor now than in the past.

The two books cannot be compared; their individual appeals vary according to whether one believes that it is better not to jump fences until they are reached or whether one accepts that to be forewarned is to be forearmed.

T. N. A. JEFFCOATE.

BRITISH MEDICAL JOURNAL
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DIETARY DEFICIENCIES AND FATTY LIVERS

Fat accumulates in the liver for one of two reasons. It may do so as a result of mobilization of fat from fat storage depots throughout the body in response to increased demands for fat combustion, as in unstabilized diabetes mellitus, and in these circumstances the chemical pattern of the hepatic fat is not altered. Or it may do so in response to liver injury or dietetic disturbance, in which case the pattern of hepatic fat is abnormal. Whenever fat accumulates in the liver owing to alterations of the diet, the cause has nearly always been traced to dietary changes which have prevented or interfered with the hepatic synthesis of phospholipids. The part played by phopholipids in fat metabolism is to transport fatty acids throughout the body, and the most important phospholipid in this respect is lecithin. Lecithin consists of glycerol to which are conjugated two fatty acids, one saturated and the other unsaturated, and the phosphate ester of the quaternary ammonium base choline, whose molecule contains three methyl groups. In the absence of lecithin from the diet fat accumulates in the liver, and it disappears when lecithin is restored. This dispersal of accumulated fat by lecithin is called its lipotropic action, and depends on the presence in the lecithin molecule of choline.

Diets deficient in choline and protein also cause fat accumulation in the liver round the central lobular vein. When this happens the formation and turnover of phospholipids in the liver are decreased and there is a hold-up in the transport of fatty acids, which are then conjugated with glycerol and deposited as neutral fat in the liver cells. Restoration of choline to the diet permits the turnover of phospholipid to start again and the incorporation of fatty acids in them, with resultant decrease in neutral fat. When fat has accumulated in the liver as a result of choline and protein deficiency, the adding of protein, but not choline, to the diet has a lipotropic effect, though it may not be sufficient to disperse all the accumulated fat. This is due to the methionine in the protein. Methionine is a sulphur-containing amino-acid which also contains a methyl group; this can be split off to form choline (methyl group donation). The lipotropic effect of proteins is partly dependent on the amount of methionine they contain.

Choline synthesis, and therefore synthesis of lecithin, can be interfered with in other ways than by the suspension of methyl group donation. For example, rats receiving diets containing adequate quantities of choline develop fatty livers when they are fed with guanido-acetic acid. This is because choline itself donates methyl groups to guanido-acetic acid to form creatine, being diverted to this from its usual role in the formation of lecithin. Similarly, the sulphur-containing amino-acids cystine and homocystine have a liver-fattening action which can be prevented by the addition of adequate amounts of choline or methionine to the diet. It is thought that this is due to the stimulation which cystine and homocystine exert on growth and appetite, causing an increased demand for choline by the organism.

In the opening pages of the *Journal* this week Professor C. H. Best and his colleagues in Toronto give experimental details confirming and extending previous work on these problems, which Professor Best also discussed in the Croonian Lecture which he gave before the Royal Society in London earlier this week. In the present paper he and his colleagues report having found that, whereas animals receiving choline-deficient diets developed fat accumulation round the central lobular veins, animals receiving protein-deficient diets developed fat accumulation in the periportal regions. Periportal accumulation of fat was not dispersed by adding choline to the diet. The different sites of fat accumulation were clearly defined only in the early stages of deficiency. When either choline or protein had been deficient for a long time, fat accumulation extended throughout the whole lobule. The significance of these findings is not clear, though Best and his colleagues think that accumulation of periportal fat when the diet is deficient in protein may be due to qualitative and quantitative alterations in the amino-acids present. They also noted a transient increase in periportal fat when an animal was transferred from a diet low in protein to one containing adequate quantities of protein and choline.

Unfortunately fatty livers in man are often the result of multiple dietary deficiencies and do not benefit from the administration of only one lipotropic factor. Furthermore, the curative merits of individual substances in human hepatic disease are hard to assess, since they are not unreasonably administered in a lipotropic blunderbuss. Professor Best's finding of periportal fat accumulation in protein-deficient rats is of special interest, because it is in those regions of the liver that fat accumulates in kwashiorkor, a perplexing disease of dietary origin which is widespread throughout the world.

SURGERY OF SIMPLE PULMONARY STENOSIS

It is now established that surgical treatment of congenital stenosis of the pulmonary valve is effective and not unduly dangerous. Pulmonary stenosis is one of the lesions which make up Fallot's tetralogy, the others being a patent interventricular septum, dextroposition of the aorta, and enlargement of the right ventricle. Pulmonary stenosis also occurs as a congenital lesion with an intact ventricular septum, in which case the term simple pulmonary stenosis is used. This is less common than Fallot's tetralogy. It is often an isolated lesion, when it is sometimes referred to as pure pulmonary stenosis. It may also occur with a patent interatrial septum (patent foramen ovale). This condition is sometimes called the trilogy of Fallot, a term which is perhaps best eschewed to avoid confusion with the tetralogy. Less usually a patent ductus arteriosus accompanies the stenosis.

Not long after the successful operative treatment of Fallot's tetralogy by anastomosis of the subclavian artery to the pulmonary artery (Blalock's operation[1]) was accepted, the alternative operation of pulmonary valvotomy was described by Sir Russell Brock[2] and Mr. Holmes Sellors.[3] The results of valvotomy in 100 cases of Fallot's tetralogy were described by Sir Russell Brock, Dr. Maurice Campbell, and Dr. D. C. Deuchar[4] recently in this *Journal* and commented on in a leading article; one-sixth of the patients died, the remainder were improved, most of them greatly. Brock and Campbell[5] have now published the results of valvotomy in 58 cases of simple pulmonary stenosis. In this series 8 patients died, but 5 of these were in the first 6 patients; good results were obtained in 46 of the 50 survivors. Many other, but mostly smaller, series have been reported, and on the whole with similar results.

In simple pulmonary stenosis, as in Fallot's tetralogy, the narrowing may lie at the valve or below it in the infundibulum. The former is more common. Occasionally both types are combined. In valvular stenosis the cusps are fused and thickened, forming a dome-like projection with a small lumen, beyond which the pulmonary artery is usually dilated. Infundibular stenosis is either a long, narrow myocardial stenosis, or less often a membranous diaphragm with a thin-walled post-stenotic chamber. The pulmonary artery may be hypoplastic. As a result of the stenosis the pulmonary circulation is diminished and the pressure in the right ventricle raised, so that this chamber hypertrophies. If the interatrial septum is intact, the arterial oxygen saturation is normal and there is no cyanosis, except occasionally peripheral venous cyanosis. A systolic murmur is heard, best at the second left interspace, and often a thrill. There may be no symptoms. The most frequent is dyspnoea, usually noticed on exertion, with reduced exercise capacity; patients also complain of easily tiring and of failure to gain weight. According to the severity of the stenosis, the heart enlarges and eventually fails. The size of the right ventricle can be assessed by fluoroscopy and confirmed by the electrocardiogram, which in advanced cases shows inversion of T-waves in the chest leads. Cardiac catheterization reveals the rise of pressure in the right heart; when the catheter passes the stenosis the pressure suddenly falls. Blood samples from various levels analysed for oxygen show no evidence of a shunt from one side of the heart to the other.

If a patent interatrial septum is present, with a functional opening allowing the passage of blood from right atrium to left, central cyanosis may occur, especially on exertion; it often leads to polycythaemia, raised haemoglobin, and clubbing of the fingers. The septal opening can be confirmed by cardiac catheterization, which will show evidence of a shunt with changes in oxygen saturation; the catheter may pass through the foramen.

Indications for surgery are not unanimously accepted. Many patients do not need operation. It is more dangerous in infancy and the adult than in childhood, or if the heart is greatly enlarged or the patient severely cyanosed. It is indicated if the symptoms are pressing, if the heart is enlarged or shows electrocardiographic evidence of right ventricular strain, or if the pressure in the right ventricle is high—say above 100 mm. Hg. The stenosis may be approached from above or from below—through the pulmonary artery or through the ventricle. The latter route has been more commonly taken, as in Campbell and Brock's series. A valvular stenosis is divided with a valvotome and enlarged with metal dilators; an infundibular stenosis must be resected with a special punch. Exact diagnosis of the level of the obstruction can be made only at operation, but it can be suspected beforehand from the radiological appearances and the pressure pattern at cardiac catheterization.[6] The adequacy of the valvotomy is best confirmed by pressure measurements at operation. F. Therkelsen[7] claims that the approach through the pulmonary artery is more direct, avoids risk of injury to coronary vessels, and allows more time. H. Swan and others,[8] dissatisfied with the

[1] Blalock, A., and Taussig, H. B., *J. Amer. med. Ass.*, 1945, **123**, 189.
[2] Brock, R. C., *British Medical Journal*, 1948, **1**, 1121.
[3] Sellors, T. H., *Lancet*, 1948, **1**, 988.
[4] Brock, R. C., *et al.*, *British Medical Journal*, 1952, **2**, 111.
[5] —— and Campbell, M., *Brit. Heart J.*, 1955, **17**, 229.
[6] Glover, R. P., *et al.*, *J. thorac. Surg.*, 1954, **28**, 481.
[7] Therkelsen, F., *Thorax*, 1955, **10**, 19.
[8] Swan, H., *et al.*, *J. thorac. Surg.*, 1954, **28**, 504.

variable results from transventricular valvotomy, have recently described transarterial valvuloplasty under direct vision, using hypothermia and temporary occlusion of the great veins so that the heart is virtually dry. They claim restoration of normal haemodynamics, and have had no deaths in seven operations.

Brock and Campbell, in their series of 58 patients, had 33 without cyanosis, of whom 1 died, and 25 with cyanosis, of whom 7 died. Operation greatly improved the colour and capacity for exercise in the survivors of this group, and reduction of right ventricular pressure was marked. Results in the acyanotic group were good in all but four. The heart was often strikingly reduced in size, and showed improvement in the electrocardiogram. There has been no evidence of recurrence of stenosis after operation; and pulmonary regurgitation has only rarely occurred, and then has not been of serious import.

NON-SPECIFIC ENTEROCOLITIS

Recent observations on non-specific inflammatory lesions of the gut involving both small and large intestines are helping to solve some clinical problems. Typically, non-specific ulcerative colitis begins in the rectum and lower sigmoid colon; it may then extend proximally to attack the whole colon. Even when the whole colon is affected the small intestine is commonly spared, though the terminal few inches of the ileum may show inflammatory changes attributed to "backwash" from the diseased colon. Regional ileitis, or Crohn's disease,[1] is classically a granulomatous lesion of the ileum in which there is mucosal destruction, thickening and contraction of the bowel wall leading to stenosis, and liability to abscess and fistula formation. The functions of the small bowel may be gravely disturbed; steatorrhoea may develop, and the patient suffer from deficient absorption of vitamins and other substances. Many authors have described patients in whom both small intestine and colon are simultaneously affected; the right side of the colon commonly shows the disease most severely—in contrast to what is usually found in ulcerative colitis. Some authors regard these cases as examples of regional ileitis extending into the colon, whereas others see them as unusual cases of ulcerative colitis affecting primarily the right side of the colon and extending proximally up the ileum.

In an important paper W. T. Cooke and B. N. Brooke[2] make a case for regarding non-specific ileocolitis as a disease in its own right. They describe a group of sixteen patients in whom both small and large intestines were affected. Some patients presented with the clinical picture and laboratory findings of steatorrhoea, but radiological examination indicated colitis. In other patients the symptoms were those of ulcerative colitis, but barium follow-through studies revealed an abnormal terminal ileum. The condition of the ileum at laparotomy or necropsy differed from that in Crohn's disease in that the bowel wall was not thickened and did not adhere to or form fistulae with other organs, and the abnormal changes were confined to the mucosa. The mucosal changes consisted of numerous small ulcers distributed throughout the distal part of the small intestine. The mucosa between the ulcers was oedematous. The authors consider these appearances to be quite different from those seen in ileitis secondary to ulcerative colitis, when "backwash" causes a uniformly granular mucosa affecting the last foot or so of the ileum.

It seems likely that ileocolitis as described by Cooke and Brooke is a different disease from Crohn's disease. It is less clear that it differs essentially from ulcerative colitis other than in its site of maximum intensity. A firm conclusion would be unwise in view of our present ignorance of the pathogenesis of ulcerative colitis, and the issue should be left *sub judice* until we have more aetiological information. From a practical viewpoint Cooke and Brooke have rendered a valuable service to clinicians who encounter these patients by stressing the need to avoid ileostomy when there is gross disease of the ileum. Unless ileostomy is being carried out as an emergency, it would perhaps be wise to have barium follow-through studies made beforehand to exclude the possibility of severe ileitis; and sometimes a fat-balance investigation may be indicated.

The medical treatment should take account of the derangement of both large and small bowels. The basic requirements are a bland low-fat diet, high in protein, giving adequate calories, correction of any electrolyte disturbances, repeated blood transfusion if the patient is anaemic, and vitamin supplements. Folic acid and large doses of calcium may be necessary if steatorrhoea is severe. Sulphonamides and antibiotics are unlikely to do more than reduce the risk of pyogenic complications. Corticotrophin or cortisone should certainly be given a trial, since these agents have been found beneficial in both regional ileitis and ulcerative colitis,[3–7] and Cooke and Brooke have given them in some cases with good effect.

[1] Crohn, B. B., *Regional Ileitis*, 1949, New York.
[2] Cooke, W. T., and Brooke, B. N., *Quart. J. Med.* (*New Series*), 1955, **24**, 1.
[3] Machella, T. E., and Hollan, O. R., *Amer. J. med. Sci.*, 1951, **221**, 501.
[4] Gray, S. J., *et al.*, *Arch. intern. Med.*, 1951, **87**, 646.
[5] Kirsner, J. B., and Palmer, W. L., *J. Amer. med. Ass.*, 1951, **147**, 541.
[6] Wirts, C. W., *et al.*, ibid., 1954, **154**, 36.
[7] Truelove, S. C., and Witts, L. J., *British Medical Journal*, 1954, **2**, 375.

DOCTORS' SMOKING HABITS

"Do as I say, not as I do" may have been a useful adage for the Victorian parent, but it is unlikely to carry much weight with the Elizabethan patient. So whether the apparent connexion between cigarette smoking on the one hand and lung cancer and coronary thrombosis on the other will lead to any significant change in popular habits will depend primarily on the seriousness with which the profession takes its own warnings. Two recent papers from Britain and the U.S.A. throw light on the present attitude of medical men in this respect. The English investigation[1] was carried out on a small scale and was confined to the 217 doctors working in Oxford hospitals. It has the peculiar merit, however, that 211 (or 97%) replied to the questionary which was sent them. From the replies it appeared that slightly over a quarter had never smoked cigarettes, while another quarter had smoked cigarettes at one time but had subsequently stopped. Of those that stopped, 18 stopped during the four years preceding October, 1950, when extensive data were first published in this *Journal* linking cigarette smoking with the development of lung cancer,[2] and 22 stopped during the following four years. Reasons for stopping were many, the numerically most important being minor ill-health and expense. Eight gave the risk of carcinoma as the principal reason. In contrast with the 40 who had stopped smoking cigarettes during the last 8 years, 11 had begun to smoke them—including 9 beginning before October, 1950. Clearly, therefore, the effect of the new evidence on doctors' smoking habits has not been great, though it would appear to have played some part in reducing the proportion smoking cigarettes from 56.9% to 47.4% over the last four years—that is, by 17% of the initial figure. That the effect has not been greater may be partly because professional opinion is not altogether agreed upon the significance of the epidemiological data. Rather more than half (57%) of the doctors were satisfied with the evidence for an association between smoking and lung cancer, but 32% were not satisfied. But it is interesting that the proportion satisfied was considerably higher among those who had never smoked cigarettes (71%) than among those who had smoked cigarettes (52%), while it was lowest of all among those who continued to smoke them (46%). Whether this is mainly because non-smokers are over-ready to believe ill of a vice they do not share, or that smokers are hesitant to condemn a personal pleasure, remains a psychological problem of some delicacy.

The reaction among doctors in the United States would appear to be similar to that in Britain.[3,4] From the much more extensive American data, which covered some 4,000 Massachusetts physicians, it appears that rather more than one-third did not smoke cigarettes. Of those who did not smoke at all, 65% accepted "that heavy smoking of cigarettes may lead to lung cancer," while among those who smoked the proportion was only 56%. Separate figures were obtained for practitioners in the different branches of medicine, and it is perhaps of significance that the highest proportions of non-smokers were found among those engaged in preventive medicine and public health and among thoracic surgeons. Among both these groups, moreover, a high proportion accepted the aetiological connexion with smoking (72% and 78% of smokers and 83% and 100% of non-smokers respectively). Of these Massachusetts physicians, 20% had reduced the amount smoked, or changed over to a pipe or cigars (that is, nearly a quarter of those who had previously been smokers); 72% of the smokers had made no change in their smoking habits. In contrast to the British doctors, the great majority of those who had changed gave as their reason the risk of carcinoma. New data obtained in this survey related to the type of advice which should be given to heavy cigarette smokers. As many as 32% of the doctors believed that they should be advised to stop smoking, 58% that they should be advised to reduce smoking with or without changing over to filter-tipped cigarettes (14%) or to a pipe or cigars (10%). But, unless more evidence appears that doctors themselves follow this advice, it may be doubted whether the public will pay much heed to it.

[1] Pyke, D. A., *British Medical Journal*, 1955, **1**, 1115.
[2] Doll, R., and Hill, A. B., ibid., 1950, **2**, 739.
[3] Snegireff, L. S., and Lombard, O. M., *New Engl. J. Med.*, 1954, **250**, 1042.
[4] —— —— ibid., 1955, **252**, 691.

BONE CHANGES CAUSED BY NERVE LESIONS

Long-standing paralysis produced by lesions of the spinal cord or nerve roots may be associated with bone changes, both in children and adults. Poliomyelitis probably affords the best example of this, a severely paralysed limb in a child often showing osteoporosis and shortening as a result of diminished and prematurely arrested local growth. Bone changes of this type are found in a number of other neurological conditions, including spina bifida and traumatic paraplegia. Their general resemblance to the skeletal changes resulting from prolonged immobilization[1-3] suggests that "disuse atrophy" is an important factor in their genesis.

Recently C. L. Jeannopoulos,[4] of New York, has directed attention to abnormal fragility of bone in this type of case and compared it with the well-known bone fragility of osteogenesis imperfecta. He describes three cases, all children, in which paralysis and sensory loss in the lower limbs resulted from lesions of the spinal cord or nerve roots; these conditions were associated with extreme fragility of bone. Repeated pathological fractures occurred, sometimes without any known injury. As other workers have noted, Jeannopoulos found that these fractures healed rapidly. Indeed, it is of interest that fractures in paraplegic patients often produce

[1] Gill, G. G., *J. Bone Jt Surg.*, 1944, **26**, 272.
[2] Green, W. T., and Anderson, M., ibid., 1947, **29**, 659.
[3] Ross, D., ibid., 1948, **30-A**, 103.
[4] Jeannopoulos, C. L., *N.Y. St. J. Med.*, 1954, **54**, 3219.
[5] Fairbank, H. A. T., and Baker, S. L., *Brit. J. Surg.*, 1948, **36**, 1.
[6] Gould, E. P., *Quart. J. Med.*, 1918, **2**, 221.
[7] Hernberg, C. A., and Edgren, W., *Acta med. Scand.*, 1949, **136**, 26.
[8] Hagelstam, L., *Acta chir. Scand.*, 1946, **93**, 169.
[9] Dent, C. E., *J. Bone Jt Surg.*, 1952, **34-B**, 266.
[10] McNeur, J. C., *Proc. roy. Soc. Med.*, 1954, **47**, 14.

very bulky masses of callus somewhat resembling the exuberant callus seen in osteogenesis imperfecta, and described by Fairbank and Baker.[5]

In neurofibromatosis, too, pathological changes in the nervous system are associated with skeletal abnormalities. In addition to the direct encroachment of expanding neurofibromata on bone, interference with skeletal development and growth, as shown by scoliosis or inequality of leg length, is sometimes observed. The immediate cause of this growth disturbance is not clear, and even more mysterious is the occasional association of another skeletal abnormality—osteomalacia—with neurofibromatosis.[6-9]

Another interesting skeletal complication of paraplegia, this time described in adult cases of long duration, is ossification in the tissues surrounding the hip-joint.[10] This lesion seems to have some relation to spasm in the flexor muscles of the hip, and sometimes extensive bony bridges appear in the muscles on the anterior aspect of the joint, completely preventing movement. The disorder is probably to be regarded as a traumatic myositis ossificans rather than a specific result of long-standing denervation.

SALIVA AND CARIES

Since W. D. Miller put forward his chemico-parasitic theory of dental caries in 1890,[11] saliva has been the focus of much speculation and research. As the initial attack of dental caries is on the tooth surface, and surface conditions are of prime importance to the process, saliva can scarcely be expected to play no part. Both the oral content of acidogenic bacteria and the buffer capacity of the saliva are correlated with the amount of dental caries. However, many other factors are involved also.

Contrary to expectations, the physical properties of saliva seem to have little influence on dental caries. The volume of saliva secreted probably has a profound effect, for extirpation of the salivary glands or diminution of their function after radiotherapy causes extensive and rampant dental caries. But measurement of the volume of saliva secreted over test periods of 5 or 10 minutes shows practically no relationship between the volume of saliva secreted and the amount of caries in the individual.

A large amount of research has produced inconclusive results or has established only low correlation between salivary contents and the incidence of dental caries. The presence in the saliva of enzymes, co-enzymes, and anti-enzymes, amino-acids, and many trace elements such as fluorine, magnesium, and chlorine, has been investigated. It is of interest, therefore, that J. C. Muhler and W. G. Shafer[12] have recently produced experimental evidence that feeding with desiccated thyroid has a marked caries-preventing effect on the rat, whereas lowering the level of the thyroid hormone in the blood with thiouracil increases the incidence of dental caries.

E. J. Ryan and S. Kirkwood[13] suggest that the probable mechanism by which the incidence of dental caries is affected is through alteration of salivary flow. They state that "a convenient explanation of the results of Muhler and Shafer would be that it is the increased concentration of iodide ion in the saliva and/or the increased saliva flow resulting from the stimulation of the degradative processes in the salivary glands that accounts for the effect of feeding desiccated thyroid," and when thiouracil was fed the increase in dental caries "may well have been caused by a decreased level of iodide in the saliva and a decrease in the rate of saliva flow." Moreover, some evidence[14-17] suggests that the salivary glands in the rat control the level of thyroid hormone in the blood stream by degrading it to iodide ion.

PRETIBIAL MYXOEDEMA

Often unrecognized, pretibial myxoedema is apt to be thought extremely rare. Moreover, only occasionally does it give rise to discomfort or disability, so that it assumes little importance in practice, though its pathogenesis is of great interest. The first description of the condition would seem to have been by P. Watson-Williams in 1895[1]; his patient was a woman with Graves's disease. Since then it has chiefly been of interest to dermatologists until Trotter and Eden[2] published their excellent paper on the subject in 1942.

Localized pretibial myxoedema seems never to appear without past or present thyrotoxicosis, and it differs from the rare lichen myxoedematosus both in this respect and in clinical appearance, for the latter condition consists of small papules filled with mucin. About 3% of patients with toxic diffuse goitre suffer from pretibial myxoedema; most commonly they are between the ages of 40 and 48, and the male–female ratio is 1:1.8 in contrast to the ratio of 1:4.4 in toxic goitre. The course of localized myxoedema is so similar to that of progressive exophthalmos that they probably have a similar aetiology.[3] In W. R. Trotter and K. C. Eden's series some patients developed both conditions simultaneously after thyroidectomy, but in half of them the pretibial myxoedema appeared before treatment of the thyrotoxicosis.

The clinical features are fairly constant. Exophthalmos is noted and the patient may be hyper- or hypo-thyroidic. R. S. M. D. Inch and C. F. Rolland[4] found that two of their three patients had gross finger clubbing. Occasionally there is indefinite aching in the

[11] Miller, W. D., *Microorganisms of the Human Mouth*, 1890, Philadelphia.
[12] Muhler, J. C., and Shafer, W. G., *Science*, 1954, **119**, 687.
[13] Ryan, E. J. and Kirkwood, S., ibid., 1955, **121**, 175.
[14] Fawcett, D. M., and Kirkwood, S., *J. biol. Chem.*, 1954, **209**, 249.
[15] —— —— *Science*, 1954, **120**, 547.
[16] Kirkwood, S., *Proc. Amer. Goiter Ass.*, in press.
[17] Thode, H. G., *et al.*, *New Engl. J. Med.*, 1954, **251**, 129.

[1] Watson-Williams, P., *Clin. J.*, 1895, **7**, 93.
[2] Trotter, W. R., and Eden, K. C., *Quart. J. Med.*, 1942, new series, **11**, 229.
[3] Curtis, A. C., *et al.*, *Arch. Derm. Syph.* (*Chicago*), 1949, **60**, 318.
[4] Inch, R. S. M. D., and Rolland, C. F., *Lancet*, 1953, **2**, 1239.
[5] Chandler, G. N., and Hartfall, S. J., ibid., 1952, **1**, 847.
[6] Zugerman, I., *New Engl. J. Med.*, 1954, **251**, 973.

legs. The lesions first appear on the antero-lateral aspect of the lower half of the legs, later extending sometimes as far as the knees and on to the back of the legs and the insteps. It is bilateral, and the skin is raised in irregular firm swellings, the surface being dimpled and faint pink or brown or unaltered in colour. Sweating at the site and the presence of coarse hairs have been noted. The lesions may disappear spontaneously in the course of years.

The aetiology is unknown. Hypothyroidism does not usually result in an increase of mucin in the skin, though the term "myxoedema" suggests that it does.[2] In pretibial myxoedema, however, a considerable amount of material is deposited which stains with thionine blue, a reaction regarded as specific for mucin. Exophthalmos does not appear to result from a similar deposition of mucin in the orbit but by retraction of the lids and oedema of the orbital tissues, though the problem of its cause is still unsolved.[5] The common factor in the causation of exophthalmos and pretibial myxoedema has been thought to be overproduction of the thyroid-stimulating hormone of the anterior part of the pituitary gland.[3 5] The hypothesis has also been suggested that localized myxoedema develops as the direct result of an unexplained insensitivity of the pretibial tissues to the action of the thyroid hormone. As Inch and Rolland[4] point out, neither hypothesis has much evidence to support it at present.

The treatment of pretibial myxoedema is unsatisfactory. Thyroxine given by mouth or injected locally, radiant heat, massage, the injection of hyaluronidase—all have proved disappointing. Inch and Rolland[4] found some temporary improvement from the combined systemic and local injection of cortisone acetate, but Zugerman[6] failed to produce any notable improvement during three months in one patient treated with hydrocortisone acetate tablets and ointment. It is clear that we are still far from understanding this curious and interesting condition.

BIRTHDAY HONOURS

The advancement of Sir Horace Evans to G.C.V.O. in the Birthday Honours will be welcomed throughout the medical profession, especially by his colleagues at the London Hospital. The services he has rendered to the Royal Family with such distinction began with his appointment as physician to Queen Mary in 1946. His signature on a bulletin reporting King George VI's health first appeared in 1949 (he received the K.C.V.O. in the same year), and thereafter he shared with the King's other medical attendants the onerous duty of caring for his Majesty in the illnesses that afflicted him until his death in 1952. Since then Sir Horace has been physician to the Queen. Two doctors who have made signal contributions to public health in this country also receive promotion: Sir John Charles, chief medical officer at the Ministry of Health, becomes a K.C.B., and Sir Alexander Macgregor, formerly medical officer of health at Glasgow, becomes a K.B.E. The conferment of a knighthood on Mr. Geoffrey Keynes, consulting surgeon to St. Bartholomew's Hospital, will give pleasure to his circle of friends and admirers both inside and outside the medical profession, for besides his attainments as a surgeon Mr. Keynes has earned distinction in the world of letters for his bibliographical and historical studies. In particular he is an authority on the poet and artist William Blake and on the portraiture of William Harvey. His contributions to surgical advancement have been unusually diverse, perhaps his principal interests being the treatment of breast carcinoma, blood transfusion, the surgery of the thyroid, and latterly the treatment of myasthenia gravis by thymectomy. In less obvious ways too he has rendered scholarly service to the profession by his devoted work at the Royal College of Surgeons, whose honorary librarian he was appointed in 1952.

Three Australians are also among the new Knights Bachelor. Mr. Albert Coates, until recently senior honorary surgeon to the Royal Melbourne Hospital, is at present Stewart lecturer in surgery at the University of Melbourne. In this capacity he has been in no small measure responsible for the establishment of the professorial chairs in medicine and surgery in the university. In the 1939–45 war Mr. Coates was senior surgeon to the Australian Imperial Force in Malaya, and his outstanding service as chief medical officer to the Allied Prisoner of War Hospital in Siam will never be forgotten by all who had the misfortune to be "guests of the Emperor of Japan" after the disaster of 1942. He has been twice president of the Victorian Branch of the B.M.A., and has played an active part in many other medical organizations. Professor Harold Dew, like Mr. Coates, is a graduate of Melbourne University. After service in the first world war he was engaged in research at the Walter and Eliza Hall Institute in Melbourne, notably with Sir Neil Hamilton Fairley. This work led to his classic monograph on hydatid disease (1928). Latterly he has been professor of surgery in the University of Sydney, and in recent years has been prominent in the development of medical education in New South Wales, at both student and postgraduate levels. He visited Britain last year as Sims Travelling Professor. Dr. Darcy Cowan graduated in Adelaide in 1908 and served throughout the first world war, for a time in the R.A.M.C. An honorary consultant physician to the Royal Adelaide Hospital, and an authority on diseases of the lungs, he was president of the South Australian Branch of the B.M.A. from 1935 to 1937. He has devoted a long professional career to the service of the community, and its recognition will be warmly welcomed by his colleagues.

Surgeon Rear Admiral S. G. Rainsford, Major-General A. Sachs, and Dr. W. E. Chiesman (of the Treasury) receive the C.B. Among those appointed C.B.E. are Professor Max Rosenheim, director of the medical unit at University College Hospital, Mr. Frederick Roques, gynaecological surgeon to the Middlesex Hospital, and two members of the B.M.A. Council, Dr. Mary Esslemont for services to medicine in Scotland, and Dr. J. A. L. Vaughan Jones for services to the Ministry of Labour; Dr. Roger Bannister also receives the C.B.E. for services to amateur athletics.

EMERGENCIES IN GENERAL PRACTICE

SERUM AND ANAPHYLACTIC REACTIONS

BY

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Almost any protein material or organic compound, by combining with body proteins, may produce severe allergic reactions. Although the use of serum and consequently the reactions from serum have been considerably reduced, these reactions still occur, and new treatments have brought new hazards. There are no more distressing emergencies than those which result from one's own treatment; their avoidance is most desirable, while their prompt recognition and treatment are essential.

It is not the purpose of this paper to discuss reactions to those substances which are used only occasionally and which only very exceptionally cause reactions, but rather to those substances which the practitioner may well use often in the course of his work. Nor is the value, or otherwise, of serum sensitivity tests dealt with, as this subject was fully discussed by Laurent and Parish in a previous refresher course series.*

There are three main types of reactions: local reactions, anaphylactic reactions, and serum sickness.

Local Reactions

An area of local redness at the site of injection of an allergenic substance is not unusual and therefore gives rise to no concern, but when such reactions are large the gap between a local and a general reaction is being narrowed, and this must be remembered if further similar injections have to be given.

Anaphylactic Reactions

Anaphylactic reactions always come on soon after the injection of the allergen, sometimes immediately, and the earlier the reaction the more likely is it to be severe and dangerous. A reaction occurring within a few minutes of the injection will be severe, and possibly fatal, while a reaction occurring after thirty minutes to an hour, although it may be quite troublesome, is rarely, if ever, dangerous.

The earliest symptoms of severe and dangerous anaphylactic reactions may be sweating, a feeling of heat throughout the body, a generalized pruritus, or an urticarial rash rapidly becoming generalized; an irritating cough, dyspnoea and wheeziness, a choking sensation, substernal oppression, or a feeling of constriction in the chest; retching or vomiting with cramp-like pains in the abdomen, sometimes diarrhoea, occasionally severe abdominal distension; and/or headache, giddiness, or sudden unconsciousness, in some cases followed by convulsions; while acute circulatory collapse and death may occur rapidly. The pulse is at first of good volume, slow and bounding, but in the dangerously ill patient it becomes rapid, weak, and thready, and there is a marked fall in blood pressure.

Serum Sickness

In serum sickness the symptoms occur only after a definite incubation period, usually six to twelve days, commonly ten days. Symptoms may be mild or severe. They consist of fever, skin eruptions, glandular enlargement, and arthritis, often in this order. The fever ranges from 99 to 104° F. (37.2 to 40° C.). Skin eruptions are the commonest manifestation, the large majority being urticarial weals or, in the severer cases, angioneurotic oedema. A morbilliform type of rash is also fairly common, and different parts of the body may present different appearances at the same time. The scarlatiniform type of rash occurs infrequently. When generalized angioneurotic oedema occurs the urine may contain albumin, but rarely blood. The presence of albumin need not cause undue concern, for after the serum disease has subsided the albumin disappears.

When severe pains in the joints occur it is almost always towards the end of the illness, and although these are a fresh and sometimes frightening addition to the patient's symptoms they usually herald the last phase, when the acute stage is nearing its end. In the more severe reactions there may be difficulty in swallowing and a feeling of a heavy lump behind the sternum, while cramp-like abdominal pains, with or without diarrhoea or vomiting or both, are also not uncommon and may last for several days.

Stiffness of the joints, especially after use, and an urticarial type of skin reaction after pressure may persist for weeks and sometimes for many months. One of my own patients, six months after his penicillin reaction, still developed pain and swelling of the feet and ankles after a brisk walk, and was unable to use his hands for heavy manual work.

Neurological complications are rare but of special interest. The commonest is an affection of the brachial plexus or part of the brachial plexus, resulting in a scapulo-humeral paralysis. The patient often complains of neuritic pains in the shoulder regions, and these are followed fairly rapidly by a flaccid paralysis with the usual tenderness and hyperaesthesia. Recovery usually occurs within six months.

Treatment of Anaphylactic Reactions

Before any therapy by injection is given, adrenaline should be near at hand; before any potent antigenic substance is used, adrenaline, intravenous aminophylline, and an intravenous antihistaminic, together with the necessary syringes, should be made instantly available. Immediately reaction occurs 5 to 10 minims (0.3 to 0.6 ml.) of adrenaline (1 : 1,000) should be injected subcutaneously. If practicable, a tourniquet should be applied above the site of the sensitizing injection, where a further 3 to 5 minims (0.2 to 0.3 ml.) of adrenaline should be injected. The dosage of adrenaline varies according to the severity of the reaction, and frequent doses may be necessary. In worsening cases the dose should be repeated in ten minutes or so and local massage used to help to expedite absorption. Intravenous adrenaline in a strength of 1 : 1,000 is contraindicated because of its danger.

In those cases not responding to adrenaline intravenous aminophylline and/or an intravenous antihistamine should be given. The intravenous aminophylline (0.48 g. in 20 ml.) should be given slowly over five to ten minutes. I have several times had most satisfactory results with this therapy. Intravenous antihistaminics—diphenhydramine hydrochloride, 50 mg., or promethazine hydrochloride, 25 to 50 mg.—must also be given very slowly. If intravenous therapy is impracticable intramuscular therapy with an antihistaminic (dosage and solutions are the same as for intravenous therapy) and/or aminophylline (0.5 g. in 2 ml.) is advisable.

Treatment of Serum Sickness

Antihistaminics and ephedrine, ½ gr. (32 mg.) three times a day or as required, are the drugs most commonly used.

British Medical Journal, 1952, **1**, 1294.

In patients confined to bed the hypnotic effect of diphenhydramine hydrochloride, 25 mg. three or four times a day, or promethazine hydrochloride, 25 to 50 mg. at night with 10 mg. once or twice a day, is helpful; in severe cases larger doses, 50 mg. up to six times in twenty-four hours of the former or 50 to 75 mg. at night with 25 mg. once or twice a day of the latter, may be indicated. For those who are ambulant antihistaminics causing drowsiness might be reserved for use at night. During the day chlorcyclizine hydrochloride, 50 mg., or phenindamine, 25 mg., may be given as required.

In severe and persistent cases which do not respond to the above measures, corticotrophin (A.C.T.H. gel) 60–80 units or cortisone 25–50 mg. six-hourly may well be indicated and are very effective. Intravenous hydrocortisone gives promise of being the most rapid form of hormonal therapy. Before considering corticotrophin or cortisone it is well to exclude the presence of a contraindication, especially a history of gastric or duodenal ulcer or of tuberculosis.

Immunization to Tetanus

In the same way as diphtheria has been reduced to a rare disease by active immunization, so can tetanus be reduced. Certainly all allergic individuals should be given tetanus toxoid, which carries for them no special risk. L. Unger gives each of his patients a card to carry with them certifying that he or she is highly allergic and has received tetanus toxoid. "In case of injury," it reads, "*do not give tetanus antitoxin*; please inject instead 0.5 ml. of tetanus toxoid."

Administration of Horse Serum

Before serum is given inquiry must be made of any previous serum therapy, of any known sensitivity to horse-dander or horse serum, and of any personal or family history of asthma, infantile eczema, hay-fever, urticaria, or food or drug allergies.

When there is a negative history intramuscular serum is, for all practical purposes, safe, but observation for half an hour afterwards is always advisable. If there has been previous serum therapy a trial dose of 0.2 ml. of the serum is given half an hour before the full intramuscular dose.

Ideally, allergic subjects should not receive serum, but when necessary those without special sensitivity to serum or horse-dander should be given 0.2 ml. of the serum diluted one in ten subcutaneously, followed in half an hour by 0.2 ml. of the undiluted serum, followed in a further half an hour by the full dose and the usual post-injection observation. Never give intravenous serum before intramuscular serum has been tried—the interval between the two is ideally two hours. (The above is essentially an abstract from the article by Laurent and Parish.)

When there is a history of previous serum and horse-dander sensitivity, preliminary testing should be with 0.05 ml. of 1 : 20 serum subcutaneously with a few minims of adrenaline followed by half-hourly injections of small but increasing doses of serum (0.1, 0.2, 0.5, 1, 2, and 4 ml., until the total amount has been given) either with a few minims of adrenaline with each dose or with adrenaline every hour or as necessary.

Skin Testing and Hyposensitization of Allergic Patients

Severe anaphylactic reactions from skin testing do occur, especially in the highly allergic individual. It is therefore advisable to carry out skin tests by the prick method before doing any intracutaneous tests.

If a known allergen can be avoided hyposensitization should only rarely be advised. Hyposensitization is widely practised for hay-fever and with other inhalant allergens causing asthma. The initial dose should be one-tenth of that which just produces a definite positive intracutaneous reaction.

The injections are given subcutaneously, usually every few days or weekly. If any constitutional reactions occur, subsequent dosage must obviously be considerably reduced and great care taken in subsequent increases. It is also important that any local reaction should be looked for and reported to the doctor before the next injection is given. If there is a local reaction the size of half a crown or more the next dose should be reduced to that which produced no reaction previously and subsequent increases in dosage made more gradually. The patient should be asked if he has a cold or sore throat or any other illness, for the presence of influenza or sore throat or other infection reduces the patient's tolerance to the allergen and it is as well temporarily to reduce the dose to at most one-tenth of that previously given, or even to omit the injection. After the infection has cleared the dose should be rapidly increased again. The dose should not be increased if the interval since the last injection is two weeks and should be reduced if the interval is over four weeks. The patient must be strongly advised not to leave the doctor's surgery for at least thirty minutes after any injection. As has already been pointed out, a reaction coming on half an hour or more after the injection is not likely to be dangerous, but one which comes on sooner usually requires immediate treatment.

It is vitally important when allergenic substances are being given that the label on the bottle should be carefully read and fully understood. If a nurse is giving such injections the doctor should check the bottle and the dose in the syringe; if a doctor has several bottles of different strengths for hyposensitization, only one at a time should be given to the nurse and the others kept under his personal care.

Another reason for constitutional reactions is too rapid absorption of the allergen, due either to the injection having been given in error intravenously or to "seepage"—that is, the rapid entrance of the allergen into small vessels pierced by the injecting needle. To minimize these possibilities, before any injection the plunger should always be pulled back and a momentary pause made to see that no blood appears. After the injection has been given firm pressure should be applied with a cotton swab immediately and for a few moments so that "seepage" into dilated vessels is unlikely. Patients should be advised against strenuous exertion for a few hours after the injection.

Reactions Following Penicillin

Severe anaphylactic reactions and death following penicillin therapy are, unfortunately, being reported with increasing frequency. The symptoms, the same as those already described under anaphylactic reactions, often come on with dramatic suddenness; the more violent reactions begin within minutes, or even seconds, of the injection. Post-mortem findings have recorded acutely distended emphysematous lungs, oedema of the glottis, and in some cases mucoid secretion in the bronchi and bronchioles.

These reactions occur more often in allergic than in non-allergic persons—that is, in those with a history of asthma, hay-fever, or of food, inhalant, or drug allergies. Those who had previous reactions from penicillin are especially at risk, particularly those with previous accelerated or immediate reactions.

Before injecting penicillin it is important to find out if the patient has had any previous penicillin therapy, any untoward incidents in connexion with penicillin, or any allergic illnesses. I do not, however, agree with the withholding of penicillin when indicated in an asthmatic unless there has been a previous reaction to penicillin.

Skin testing as a means of excluding those at risk is not altogether satisfactory, for a negative skin test does not invariably exclude a serious reaction, nor does a positive reaction indicate that an anaphylactic reaction will always occur. In view of the difficulties and lack of precision inherent in skin testing, Siegal has suggested giving orally a penicillin tablet (50,000 units) ten minutes before the intramuscular injection. Another practical suggestion is to inject at first only a drop or two of penicillin and wait for

forty-five seconds before completing the injection, in order to try to avoid those particularly severe reactions that come on suddenly. Injecting in the arm rather than in the buttock is also recommended so that a tourniquet can be applied if necessary.

"Serum sickness" reactions following penicillin therapy are now widely known and recognized. The incubation period and symptoms are exactly the same as in the classical serum disease, and in the same way the severity varies widely. Although penicillin is non-toxic, its administration carries a risk of hypersensitivity estimated at 2–8%.

The indiscriminate use of penicillin is to be condemned, for reactions occurring when there is little indication for penicillin are indeed unfortunate, nor must we forget the possible sensitizing effect of initial injections. It has been suggested that procaine penicillin is more allergenic than crystalline penicillin, but some authorities are not of this view.

Reactions to Insulin

Severe generalized systemic reactions are very rare, and so far as I know death has not been recorded. Reactions usually consist of local redness and swelling with pruritus which may be quite troublesome but which usually subsides after a few weeks with the continuation of insulin. Antihistaminic drugs are helpful, both prophylactically and for symptomatic relief, until spontaneous recovery occurs.

Reactions to Bee- and Wasp-Stings

The frequency of death from a bee- or wasp-sting is difficult to estimate, although such reports in the lay press are not unusual. The post-mortem findings are the same as those found in anaphylactic deaths from other antigens —laryngeal oedema and acute pulmonary emphysema. The early signs and symptoms are the same as those occurring in any severe anaphylactic reaction.

Successive reactions often become progressively worse, and those who are allergic to bee- or wasp-stings should be advised of this possibility. Every person who knows that he is allergic to bee- or wasp-stings should do all he can to avoid being stung. If this risk cannot be avoided, he should carry with him some tablets of ephedrine (½ gr.) or isoprenaline sulphate (20 mg.) and an antihistamine such as chlorcyclizine hydrochloride (50 mg.). If he is stung he should at once take one or two tablets of ephedrine (or half to one and a half tablets of isoprenaline) and one or two tablets of the antihistamine. Successful hyposensitization has been carried out in individual cases and a scheme of hyposensitization is given by Mueller and Hill.* Bee venom is an extremely potent antigen, and such procedures may well be left to experts. Further work is required on bee and wasp hyposensitization before the risks and benefits can be accurately assessed.

Miscellaneous Reactions

Reactions to vaccines prepared from chick embryos, such as most influenza, typhus, and yellow-fever vaccines, have been observed in individuals who are extremely allergic to egg; in these patients avoidance of such vaccines is necessary.

That occasional but rare reactions to local analgesics such as cocaine occur has long been recognized, and before carrying out bronchograms sensitivity tests are common practice.

Severe anaphylactic reactions following the injection of vitamin B have been recorded, and indicate the advisability, whenever practicable, of giving therapy by mouth rather than by injection.

Next article on Emergencies in General Practice.—"Uterine Inertia," by Mr. Clifford Kennedy.

New Engl. J. Med.*, 1953, **249, 726.

MEDICAL BIRTHDAY HONOURS

The names of the following members of the medical profession were included in a Birthday Honours List published in *Supplements* to the *London Gazette* on June 9:

G.C.V.O.

Sir HORACE EVANS, K.C.V.O., M.D., F.R.C.P. Physician to Her Majesty the Queen.

K.C.B. (Civil Division)

Sir JOHN ALEXANDER CHARLES, M.D., F.R.C.P., D.P.H. Chief Medical Officer, Ministry of Health, Ministry of Education, and Home Office.

K.B.E. (Civil Division)

Sir ALEXANDER STUART MURRAY MACGREGOR, O.B.E., M.D., LL.D., F.R.F.P.S., D.P.H. Medical Officer of Health for Glasgow from 1925 to 1946. For services to public health in Scotland.

Knighthood

ALBERT ERNEST COATES, O.B.E., M.D., M.S., F.R.C.S., F.R.A.C.S. For services to the medical profession in Australia.

DARCY RIVERS WARREN COWAN, M.B., B.S., F.R.A.C.P. Honorary Consulting Physician, Royal Adelaide Hospital.

HAROLD ROBERT DEW, Sc.D., M.B., B.S., F.R.C.S., F.R.C.S.Ed., F.R.A.C.S., Professor of Surgery in the University of Sydney. For services to medicine in Australia.

GEOFFREY LANGDON KEYNES, M.D., F.R.C.P., F.R.C.S., F.R.C.O.G. Consulting Surgeon, St. Bartholomew's Hospital.

C.B. (Military Division)

SEYMOUR GROME RAINSFORD, D.S.C., M.D., D.P.H. Surgeon Rear-Admiral. Honorary Physician to the Queen.

ALBERT SACHS, C.B.E., M.D., M.R.C.P. Major-General, late R.A.M.C. Honorary Physician to the Queen.

C.B. (Civil Division)

WALTER ERIC CHIESMAN, M.D., F.R.C.P. Medical Adviser, H.M. Treasury.

C.M.G.

BENJAMIN KEITH RANK, M.B., M.S., F.R.C.S., F.R.A.C.S. Chief Plastic Surgeon, Heidelberg Military Hospital, Victoria, Australia.

ALLAN ROBERT STANLEY VICKERS, O.B.E., M.B., Ch.M. For services to the Flying Doctor Service in Australia.

C.B.E. (Military Division)

ALBERT FREDERICK COOK, O.B.E., L.R.C.P.&S.I., D.P.H. Air Commodore, R.A.F.

ALLEN LEPARD CROCKFORD, D.S.O., O.B.E., *M.C.*, T.D., M.B., B.Chir. Brigadier, late R.A.M.C., T.A. Honorary Surgeon to the Queen. Secretary to St. Thomas's Hospital Medical School.

C.B.E. (Civil Division)

ROGER GILBERT BANNISTER, M.B., B.Chir. For services to amateur athletics.

PHILLIPPE LESLIE CARO CARRIER, M.D., M.R.C.P., D.P.H. Senior Medical Officer, Home Office.

CHARLES WILLIAM ATKINSON EMERY, M.B., B.Ch. Principal Medical Officer, Ministry of Pensions and National Insurance.

MARY ESSLEMONT, LL.D., M.B., Ch.B., D.P.H. General Council Assessor to the University Court of the University of Aberdeen since 1947. President of the Medical Women's Federation, 1953–4. For services to medicine in Scotland.

RICHARD THOMAS BONDFIELD GREEN, M.D., D.Sc., D.T.M. Senior Bacteriologist, Institute for Medical Research, Federation of Malaya.

JOHN LEWERS GROVE, M.D. A prominent physician in Launceston, Tasmania.

JOHN ARTHUR LLEWELYN VAUGHAN JONES, M.B., Ch.B. Regional Medical Adviser, East and West Ridings Region, Yorkshire. For services to the Ministry of Labour and National Service.

WILLIAM CALDWELL MCCLELLAND, M.B., Ch.B. For services to sport in Australia.

FREDERICK GRANTLEY MORGAN, M.B., Ch.B. Director, Commonwealth Serum Laboratories, Royal Park, Victoria, Australia.

FREDERICK WILLIAM ROQUES, M.D., M.Chir., F.R.C.S., F.R.C.O.G. Consultant in Gynaecology to the Royal Air Force. Obstetric and Gynaecological Surgeon, the Middlesex Hospital and the Royal Masonic Hospital. President of Section of Obstetrics and Gynaecology, Royal Society of Medicine, 1954–5.

MAX LEONARD ROSENHEIM, M.D., F.R.C.P. Professor of Medicine in the University of London and Director of Medical Unit at University College Hospital Medical School.

JAMES LESLIE ALLAN WILL, M.B., Ch.B., F.R.C.S.Ed., F.R.A.C.S. Orthopaedic Surgeon, Christchurch General Hospital, New Zealand.

M.V.O. (Fourth Class)

WILLIAM HILGROVE LESLIE MCCARTHY, D.S.O., *M.C.*, M.D., M.R.C.P., D.P.H. Coroner to the Queen's Household.

O.B.E. (Military Division)

GEORGE GREGG, M.D., F.R.C.P.I. Lieutenant-Colonel, R.A.M.C., T.A. Consulting Physician in Physical Medicine in charge of Department of Physical Medicine and School of Physiotherapy, Royal Victoria Hospital, Belfast.

LILIAN GERTRUDE MOORE, M.B., B.Ch., M.R.C.P.Ed. Wing Commander, R.A.F.

WILLIAM MUIR STEWART, M.B., B.Ch., D.P.H. Lieutenant-Colonel, R.A.M.C.

JAMES CLARKE TAYLOR, M.B., Ch.B., F.R.C.S., D.P.H., D.I.H. Wing Commander, R.A.F.

ALISTAIR ROBERT CAMERON YOUNG, M.R.C.S., L.R.C.P., D.M.R.D. Wing Commander, R.A.F.

O.B.E. (Civil Division)

WILLIAM ROY BILLINGTON, M.D. For medical services in Uganda.

ARTHUR DOUGLAS BRIGGS, M.B., Ch.B. Medical Superintendent, Stobhill Hospital, Glasgow.

DAVID ERIC CAMERON MEKIE, M.B., Ch.B., F.R.C.S.Ed. Professor of Surgery in the University of Malaya.

SIMON EZIEVUO ONWU, M.B., Ch.B., D.T.M.&H. Deputy Director of Medical Services, Eastern Region, Nigeria.

EDWIN ALFRED TRIM, M.D., D.T.M.&H. Deputy Director of Medical Services, Kenya.

M.B.E. (Military Division)

CLARK NICHOLSON, *M.C.*, M.D. Major, R.A.M.C., T.A. Honorary Surgeon, Moreton-in-Marsh District Hospital.

CHARLES GEOFFREY WHITE, B.M., B.Ch. Squadron Leader, R.A.F.

M.B.E. (Civil Division)

NEVILLE GEORGE DAVID CAMPBELL, B.M., B.Ch. Medical Officer, Sierra Leone.

DONALD GORDON DUFF, *M.C.*, M.B., Ch.B., F.R.C.S.Ed. Surgeon-Superintendent, Belford Hospital, Fort William, Inverness-shire.

MOHAMED FAQUIR, Medical Officer, Uganda.

SAMUEL MAURICE BARKLIE HILL, M.B., B.Ch. Regional Medical Officer, Northern Region, British European Airways.

ABIEZERI KYABASINGA KIBAYA, Medical Officer, Uganda.

VISHWANATH SITARAM NIJASURE. Senior Sub-assistant Surgeon, Tanganyika.

JOHN TODD, *M.C.*, D.F.C., M.B., Ch.B. For medical and missionary services in Northern Rhodesia.

Miss Ina Lindsay Cook, M.A., LL.B., Assistant Secretary of the Royal College of Physicians of London, has been appointed M.B.E. (Civil Division).

Nova et Vetera

ROYAL SOCIETY OF MEDICINE SESQUICENTENNIAL

History has a habit of repeating itself, with necessary variations. Fifty years ago, on May 27, 1905, the then Prince of Wales (afterwards George V) was admitted an Honorary Fellow of the Royal Medical and Chirurgical Society, shortly afterwards to change its name by supplemental charter to "Royal Society of Medicine." There followed a banquet which we are told in the official history was a "tremendous success," attended by 457 Fellows and guests. On June 7, 1955, the Duke of Edinburgh was similarly admitted an Honorary Fellow, and again there was a banquet, this time with an attendance of close upon 1,000. The President 50 years ago was Sir Richard Douglas Powell; on this recent occasion he was Sir William Gilliatt.

The Duke of Edinburgh declared once again his admiration for the medical profession; he said that he believed the whole essence of medicine to lie in the personal relationship between doctor and patient. He was prepared to put up with all the disadvantages and perils of this age—strikes and the threat of the H-bomb—"if I can be looked after by the kind and brilliant men around me." He went on to propose the health of the Society, which was responded to by Sir Francis Walshe, the immediate past president. Sir Francis described the Society as the inheritor and hard-pressed sustainer of the greatest medical library in the Old World as well as of an extremely active forum for the exchange of medical knowledge by discussion and communications, oral and written.

To the toast of "The Guests," proposed by Sir Arthur Porritt, there were two replies, one from the Marquis of Salisbury, Lord President of the Council, and the other from Lord Adrian, President of the Royal Society. The former paid a tribute to medical research, while the latter, in praising the Royal Society of Medicine, said that if it were dissolved there would be no immediate dramatic change in medical services, yet the loss would be immeasurable.

History of the Society

One feature of the dinner was the presentation to the Duke of Edinburgh of a copy of the handsome volume which has been written to commemorate the occasion.[1] The author is a medical historian of distinction, Dr. Maurice Davidson. His book takes us back to the origin of the Society, which was not 50 but 150 years ago. It began its life in a tavern in 1805, when 26 disgruntled members of the Medical Society of London, indignant at the autocracy of the seemingly irremovable president, one James Sims, decided to form a new society to be called the Medical and Chirurgical Society of London. Among those present at that determined meeting were John Abernethy and Sir Astley Cooper, but the real founders were William Saunders, the first president, Alexander Marcet, and John Yelloly, the first secretary, all Fellows of the Royal Society. The early meetings were held at Verulam Buildings, near Holborn. On May 28, 1806, a paper by Dr. Pearson, on the treatment of hooping cough [*sic*] was discussed, and a fortnight later the Society had a field night with discussions on tinea capitis, chronic croup, and the use of cold in gout, as well as a note on hydrophobia in a horse. The picture is in odd contrast with the sectional meetings of to-day, where, to take the most recent diary card, there are discussions in one week on the bacteriological diagnosis of pertussis, on antibiotics in bacillary dysentery, on intramuscular administration of "penidural," and on the treatment of paraplegic bladder.

The Royal Medical and Chirurgical Society—it became "Royal" in 1834 and William IV was its first patron—presently was concerned with bringing about a union with itself of the various specialist societies which began to be formed in the latter half of the nineteenth century. It took a lot of doing. In 1870, for example, some of the societies were prepared to come in, but others trembled on the brink. The idea was to have a comprehensive society under some such high-sounding name as the "Royal Academy of Medicine." The word "Academy" was still favoured by many, even down to the time of the actual amalgamation. This was in 1904, when at a meeting held at the Royal College of Physicians, with Sir William Church in the chair, 150 members of different societies resolved to fuse their societies into 16 sections in the newly named Royal Society of Medicine. The sections now number 26, the youngest being the Section of General Practice.

The Society's House and Library

Having got the name, it remained to find the local habitation. Some still living will remember the old meeting-place at 20, Hanover Square, now a commercial house. This building had been acquired by the Society in 1899, but very soon new premises were sought. A site was acquired at the corner of Wimpole Street and Henrietta Street, and the

[1] *The Royal Society of Medicine. The Realization of an Ideal. 1805–1955.* Published by the Royal Society of Medicine. Price £1 1s.

great building arose which was opened by George V in 1912. It appeared at the time to be ample for all the Society's needs, with its two meeting halls, its council chamber and committee-rooms, and the noble reading-room for the library. Sir Francis Walshe recalled the fact at the dinner the other evening that there were at that time 20 dressing-rooms where Fellows could change. But even then some far-seeing persons saw that future extension might be necessary, and provision was made for the raising of the roof. An extra floor was added, through the generosity of the Wellcome Trust, during Lord Webb-Johnson's presidency in 1950–2. It was certainly needed if only to house the ever-expanding library, which now contains over a quarter of a million volumes, has 50,000 occupants in the course of a year, and employs a staff of 26. What a contrast to the library at the time the Medical and Chirurgical Society was founded. It had between 400 and 500 books, was open two hours a week, and two books were allowed each member at one time. The Duke of Edinburgh was told that, like any other Fellow, he could now take out eight books at once.

Of the many personalities connected with the Society one name stands out conspicuously, that of Sir John Macalister, its secretary for 38 years. His work for the Society was a life's devotion; his hand was felt in every part of its organization, *Proceedings*, and library and all. To him is due perhaps more than to anyone else the successful emergence of the Society 50 years ago into a body covering every branch of medical practice and research. He was succeeded in the secretaryship in 1925 by Mr. Geoffrey Edwards, selected out of 462 applicants, under whom the Society flourished yet more and made several successful new ventures.

Dr. Davidson's commemorative volume ends with brief biographies of the 24 Presidents of the Society since 1907. To name only those who have passed on, and only a few of those—William Selby Church, Humphry Rolleston, John Bland-Sutton, StClair Thomson, James Berry, Dawson of Penn. The Society has been fortunate in commanding the disinterested service of some of the most distinguished medical men in succeeding generations.

APPROVED NAMES

Approved names are devised or selected by the British Pharmacopoeia Commission, and the intention is that if any of the drugs to which these approved names are applied should eventually be described in the *British Pharmacopoeia* the approved name should be its official title. The last supplementary list of approved names was published in the *Journal* of October 30, 1954 (p. 1045).

Approved Name	*Other Names*
Chlorhexidine	Bis - *p* - chlorophenyldiguanidohexane. "Hibitane."
*Diethylthiambutene	3-Diethylamino-1 : 1-di-2'-thienylbut-1-ene. "Themalon."
*Dimethylthiambutene	3-Dimethylamino-1 : 1-di-2'-thienylbut-1-ene.
*Ethylmethylthiambutene	3-Ethylmethylamino-1 : 1-di-2'-thienyl - but-1-ene.
Methyl phenidate	Methyl 1 - phenyl - 2 - piperidylacetate. "Ritalin" is the hydrochloride.
†Phenindione	2-Phenylindane-1 : 3-dione. Phenylindanedione. "Dindevan."
Polymyxin	Antimicrobial substances produced by *Bacillus polymyxa*. (Specific substances are designated by a terminal letter; thus, polymyxin E.)
Streptonicozid	A compound formed by interaction of a suitable streptomycin salt and isoniazid. "Streptohydrazid."
Tripolidine	*trans* - 1 - 2'-Pyridyl-3-pyrrolidino-1-*p*-tolylprop-1-ene. "Actidil" is the hydrochloride.

*Not intended for use in human medicine; diethylthiambutene is of interest in veterinary medicine.
†Replaces phenylindanedione as the approved name.

Correspondence

Coal-workers' Pneumoconiosis

SIR,—Dr. Horace Joules, in his letter (*Journal*, May 14, p. 1222) commenting on our article (*Journal*, April 23, p. 994), asks for the evidence on which "approved conditions" are based. When the Industrial Injuries Act came into force in 1948, provisional figures for approved levels of dustiness (in terms of particles of respirable size per cubic cm.) were agreed by the various interested parties after reviewing all the evidence, including that contained in the M.R.C. Special Reports Nos. 243 and 244 on "Chronic Pulmonary Disease in South Wales Coal-miners."[1,2] Evidence that the provisional figures are indeed low enough can only be obtained by following up, by periodic *x*-ray examination, groups of miners in representative pits in all parts of the country in which continuous surveys of dust conditions are also being made. This is being done as part of the Pneumoconiosis Field Research Scheme of the National Coal Board, which is by far the most ambitious field investigation in pneumoconiosis being undertaken in any part of the world. As pneumoconiosis appears and progresses so slowly it is inevitable that a number of years must elapse before any valid conclusions can be drawn, but the earliest opportunity is being made to get an indication of the adequacy of the provisional figures by study of our own follow-up surveys, some of which now extend over a period of more than five years.

In his second paragraph Dr. Joules suggests that reliable figures for morbidity from chronic bronchitis are available nationally and it should, therefore, be possible to assess the effect of mining on this disease. We are actively investigating the problem, but believe that the answers are less easily obtained than his letter suggests. The national statistics apply to spells of sickness and not to individuals, and not to those over the age of 65, and thus do not include all retired miners, and they are also unfortunately not available broken down by occupation within the regions. As there are big differences in the mortality figures from chronic bronchitis in different areas, we believe that if we are to obtain reliable information it is necessary to compare miners and ex-miners with other men living in the same community who have never worked underground. Two community surveys of this type have been made—one in South Wales and one in Lancashire—and the results will be published shortly. The findings in these two areas are quantitatively different and, therefore, suggest caution is necessary in generalizing too widely from investigations in one area. Dr. A. L. Cochrane has recently analysed the death rates in relation to the category of pneumoconiosis in his "follow-up" of the Rhondda Fach. This also will be published shortly.

We support fully Dr. Joules's plea for a more intensive drive to eliminate tuberculosis from the mines, but we doubt whether it is practicable to employ the method used in the Rhondda Fach (which was essentially a research project) on a much wider basis. Success in eliminating tuberculosis by treating all infectious cases can only be achieved if all these are detected, which requires *x*-raying a very high proportion of the community. We wonder whether it would not be a good policy to follow the example set in certain States of Australia, where periodic *x*-ray examinations of the chest have been made compulsory in the community and, as a result, a much higher proportion of the population has been examined than was possible previously on a voluntary basis.

Dr. H. R. Thomson's description (*Journal*, May 21, p. 1280) of the type of chest pain among the Durham miners with pneumoconosis coincides exactly with our observations in South Wales. We agree the symptoms are much commoner in the miners, and particularly those with complicated pneumoconiosis, than in cases of emphysema and bronchitis. We are often uncertain of its cause. It would be interesting to know whether it is related to the degree of pulmonary hypertension.—We are, etc.,

Penarth, Glam. J. C. GILSON.
G. S. KILPATRICK.

REFERENCES

1 *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, 1942, No. 243.
2 Ibid., 1943, No. 244.

Vagotomy with Gastroenterostomy for Duodenal Ulcer

SIR,—In their interesting article on "Vagotomy and Gastroenterostomy for Duodenal Ulcer" (*Journal*, May 14, p. 1183) Mr. M. J. Bennett-Jones and Mr. S. O'Domhnaill mention a patient, Mrs. M. B., aged 58, upon whom Professor Wells recently performed a revision gastrectomy operation, her fourth operation. Mr. Bennett-Jones agrees that it would be interesting to record the result of this procedure.

In 1951 vagotomy and gastroenterostomy were performed for duodenal ulcer. This was followed by epigastric pain unrelated to food, but relieved by the vomiting of bile. The gastroenterostomy was converted to a Billroth II gastrectomy, and this was later altered to a Billroth I anastomosis without improvement in the symptoms. In October, 1954, the gastrectomy was revised to the Roux-en-Y type. Pain and bile vomiting were immediately relieved, and the patient has, so far, remained free from dyspepsia. She has gained two stones in weight since the last operation.

It is our belief that certain cases of bilious vomiting following Polya gastrectomy are due, in part at least, to pre-existing retraction of the cardia with incompetence of the cardio-oesophageal sphincter mechanism. In such cases the operations of enteroanastomosis or jejunoplasty, which still allow bile to enter the stomach, may fail to relieve the symptom. Conversion of the gastrectomy to the Billroth I type, whilst improving an associated deficiency state, also permits bile reflux into the stomach and thence to the oesophagus. In the last year we have, in 12 cases of severe bilious vomiting after gastrectomy, diverted the duodenal contents from the stomach and provided free drainage of the afferent loop by conversion of the anastomosis to the Roux-en-Y type. If not already performed, abdominal vagotomy is also carried out.

The failure of this patient to gain relief from any procedure other than the Roux anastomosis seems to us to support the belief that gastro-oesophageal reflux was an essential factor in the causation of her symptoms. Attention has already been drawn to this possible combination of circumstances.[1] The series of twelve cases mentioned above, which overlaps those already reported, will be presented as a separate communication.—I am, etc.,

J. H. JOHNSTON.

Liverpool, 3.

REFERENCE

1 Wells, C. A., and Johnston, J. H., *Lancet*, 1955, 1, 937.

"Half-minute" Thermometers

SIR,—Your correspondent Dr. P. Gilbert (*Journal*, May 7, p. 1158) has raised a point of great importance. It is known that the times stamped on clinical thermometers bear no useful relation to the time taken to reach a constant reading, but it is not nearly well known enough to medical men and nurses. It is such a commonplace to have a thermometer inserted only for a bare half-minute that one cannot help having serious doubts about the value of temperature records in many hospitals, and in much of general practice. This trade practice of marking unrealistic times on clinical thermometers has been unfavourably commented on before, and it is time it was dropped.

May I suggest a standard "time-in-mouth" of two minutes? It would be easy to test all hospital thermometers, new or old, at two and five minutes in a constant-temperature bath under standard conditions. Any rising more than 0.1° F. after two minutes should be returned to the makers.

There is a related matter which seems to me worth attention. According to Best and Taylor[1] the range of normal oral temperatures in humans is 96.6°–100° F. (35.9°–37.8° C.). The medical profession seems to assume that the normal in *all* human beings is 98.4° F. (36.9° C.). This is inevitable in hospitals for new patients, never seen in health, and as a first approximation in general practice. Is it too much to expect one's practitioner to have some more accurate idea of one's normal temperature, especially when there are signs—for example, a high or low B.M.R.—pointing to "abnormal normality"? (This is not a rhetorical question.)

These two factors combined, it seems to me, could lead to errors in diagnosis, possibly serious errors. I write from some experience; it is particularly irritating to be told, when feeling rather ill, that at 99.8° F. (37.7° C.) one has "not really got a temperature," when (*a*) it is really 100.6° F. (38.1° C.), and (*b*) one's normal figure is 97° F. (36.1° C.).—I am, etc.,

London, W.5. D. J. CAMPBELL.

REFERENCE

1 Best, C. H., and Taylor, N. B., *The Physiological Basis of Medical Practice*, 1955, 6th ed., p. 730. Baillière, London.

Potassium Permanganate Ulceration

SIR,—Further to the article by Drs. E. A. J. Alment and C. S. Nicol (*Journal*, October 3, 1953, p. 759) and the subsequent correspondence (*Journal*, October 31, 1953, p. 994), it may be of interest to record another instance of the misguided use of tablets of potassium permanganate as an abortifacient.

I saw recently a girl of 17 who said she had been bleeding profusely per vaginam since the morning and had passed many large clots; this was accompanied by severe continuous pain in the hypogastrium and she thought she was pregnant. Her last menstrual period had begun about five weeks previously and she had never been pregnant before. On examination she was poorly nourished and somewhat shocked; there was moderate rigidity to palpation in both lower abdominal quadrants, but no evidence of peritoneal irritation or of free fluid in the abdomen. Vaginal examination was inconclusive owing to lack of co-operation. Under anaesthesia several handfuls of clotted blood were removed from the vagina and the true state of affairs revealed. There was no pregnancy in the uterus, which was rather small, with a long thin cervix and nulliparous external os. The whole of the right lateral fornix and the vaginal wall on the same side were denuded of epithelium and presented several scattered black eschars. The right side of the cervix was largely eroded, leaving an area of deep ulceration with irregular but sharply defined margins terminating medially at the external os in a black eschar the size of a farthing and shading off laterally into the more superficial ulceration in the fornix. The following morning the haemoglobin was found to be 5 g.%, and the girl revealed that she had been given some tablets by her cousin which she had inserted herself and soon after had noted the onset of pain and bleeding.

Discussion with my colleagues confirms that this is not an unfamiliar clinical entity locally, and no doubt its popularity with the ignorant is due in part to the rapid onset of severe bleeding which follows insertion of the tablets. I am grateful to Dr. Edward I. Salisbury, medical director, United Fruit Company, Boston, for permission to publish.—I am, etc.,

Panama. C. C. EWING.

Status Bonnevie-Ullrich

SIR,—Drs. J. B. Barlow and S. E. Levin (*Journal*, April 9, p. 890) in their article on status Bonnevie-Ullrich assert:

"In over a hundred patients reported in the English language literature, however, we have found reference to oedema in only two case reports. Silver (1951) stated that the feet of his patient, aged 2 years and 8 months, were described as having been 'swollen' at birth; and Vulliamy (1953), in his report of an 8-year-old girl, described 'unexplained oedema of hands and feet at birth, persisting in the feet for the first three years.' Pitting oedema was a very prominent feature in our patient and was, in fact, the reason that the mother sought medical advice. It is difficult to understand how, if it were present, such a conspicuous abnormality could have been so frequently overlooked. Ullrich (1949), however, stated that the swelling disappears during the first two years of life. As our patient is the first under the age of 2 years whose case is described in the English literature this may well explain why oedema has so seldom been mentioned."

Permit me to draw their attention to two important inaccuracies and to refer them to my article, "The Bonnevie-Ullrich Syndrome," published in the *Australian Medical Journal*.[1] In the case I published there was marked congenital lymphangiectatic oedema of the dorsum of the hands and feet, and, moreover, my patient was under 2 years of age. Therefore, when they state that in over 100 patients reported in the English language literature they found refer-

ence to oedema in only two case reports, they were incorrect in so far as my case brings the total to three cases. Furthermore, they are incorrect in asserting that their patient is the first under the age of 2 years to be described in English literature, as my patient was only 13 months.—I am, etc.,

Broken Hill, New South Wales, Australia. MICHAEL ELYAN.

REFERENCE

1 Elyan, M., *Med. J. Aust.*, 1954, **1**, 710.

Idiopathic Pulmonary Haemosiderosis

SIR,—Further to Dr. J. M. Cliff's letter (*Journal*, May 28, p. 1340), cases of idiopathic pulmonary haemosiderosis in adolescents are reported by Waldenström[1] and Walton and Williams[2] in which recurrent acute episodes resulted in death after about three years. These cases are similar to the original descriptions of the condition in children.

The cases described by Kerley,[3] Cliff,[4] and in my recent article (*Journal*, April 23, p. 1008) differ in showing long periods with minimal symptoms and no anaemia, though some had initial acute attacks. It is in these that it is suggested that the outlook is generally good. Clarification of the prognosis must, of course, await the publication of additional cases.—I am, etc.,

London, N.W.8. N. A. J. HAMER.

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1 Waldenström, J., *Acta radiol. (Stockh.)*, 1944, **25**, 149.
2 Walton, M., and Williams, A. A., *British Medical Journal*, 1951, **2**, 390.
3 Kerley, P., in *Textbook of X-ray Diagnosis*, 1951, edited by S. C. Shanks and P. Kerley, 2nd ed., vol. 2, p. 178. London.
4 Cliff, J. M., *Brit. J. Radiol.*, 1953, **26**, 102.

Megaloblastic Anaemia following Anticonvulsants

SIR,—The interesting article on two cases of megaloblastic anaemia following anticonvulsants by Dr. N. Berlyne, Dr. M. Levene, and Dr. A. McGlashan (*Journal*, May 21, p. 1247) prompts me to publish a preliminary note on similar observations on two patients treated with primidone.

(1) A woman, aged 37, was first seen by me on May 1, 1954, when she gave a typical history of temporal lobe epilepsy of 13 years' duration. Barbiturates and bromides had not controlled her fits, and she was therefore changed over to tab. primidone 250 mg. three times a day on May 4. Four and a half months later her general practitioner requested a consultation on account of the patient's lassitude, anorexia, weight loss, ulcerative gingivitis, and stomatitis. The fits had ceased. The patient appeared rather ill on September 15, when she had a smooth tongue, stomatitis, and a blood count as follows: red cells 1,420,000; haemoglobin 37%; colour index 1.3; white cells 4,550. A number of late megaloblasts were seen in the film. The bone marrow was megaloblastic. Free hydrochloric acid was present on gastric analysis. Glucose tolerance, fat balance, and liver function tests were within normal limits.

Folic acid 20 mg. daily was commenced on September 17, with a good reticulocyte response. On November 23 red cells numbered 4,500,000 with a haemoglobin of 91% and a colour index of 1. Folic acid was discontinued that day. Since admission to hospital she had received no primidone. This was, however, restarted on January 7, 1955, without addition of folic acid. Full blood counts have been carried out every fortnight since. On May 17 her red cells numbered 4,250,000, the Hb 94%, and the colour index was 1.1. The red cells appeared macrocytic.

(2) A woman aged 44. This patient gave a history of epileptiform fits since 1950, caused by an oligodendroglioma of the left hemisphere, proved on biopsy and treated by *x*-ray. Epilepsy persisted after *x*-ray treatment, but was much better controlled after September, 1952, when she was put on tab. primidone twice daily. In January, 1953, the dose was increased to four tablets daily, and prior to admission to hospital on February 3, 1955, she had taken five tablets daily. No phenytoin or any other drug was given to her after September, 1952. In autumn, 1954, she began to feel tired, lost her appetite, had dizzy spells, and became dyspnoeic. Her private doctor (Dr. Gibson) arranged for a blood count (December 2, 1954), which was as follows: red cells 1,200,000; haemoglobin 32%; colour index 1.3; film: occasional early and late megaloblasts seen. She was thought to be a case of pernicious anaemia, and received first "cytamen" and later "anahaemin" injections without benefit. A blood count on February 2, 1955, was reported as: red cells 1,030,000; haemoglobin 22%; colour index 1.1; white cells 4,850. She entered hospital on the following day, and was so ill that she had several pints of blood during the first week. A fractional test meal showed free hydrochloric acid. The bone marrow was megaloblastic. Fat balance tests in the faeces gave normal results. The liver function tests were normal. She received 20 mg. folic acid daily as well as 750 mg. primidone from the day of admission. There was a good reticulocyte response and she recovered steadily. Her blood count at the end of April was: red cells 4,360,000; haemoglobin 92%; colour index 1.05; white cells 5,300. The patient left the hospital on April 25. The treatment was then changed from primidone to barbiturates with the intention of continuing so well beyond the period of protective effect of folic acid previously given. It is planned to prescribe primidone again later without additional folic acid but with the safeguard of fortnightly blood counts as in the case of our first patient.

Primidone is now widely used all over the world, and it was therefore somewhat of a surprise to find only one case of megaloblastic anaemia following primidone published by Chalmers and Boheimer.[1] This patient, however, had previously received various other anticonvulsants, including phenytoin. Case 2 of Berlyne, Levene, and McGlashan also had phenytoin until three to four months prior to development of a severe degree of anaemia. I entirely agree with the writers that the effect of phenytoin and primidone leading to a megaloblastic anaemia seems most probable in their cases, but further definite proof of this relationship is desirable.

Dr. Moorhouse and I hope to be able, by continued clinical and haematological review of the two patients mentioned in this paper, to obtain more detailed information about the potential danger of a most valuable drug in the treatment of epilepsy. Our two patients seem to be particularly suited for the investigation related to primidone, as no phenytoin had been prescribed previously in either case.—I am, etc.,

Liverpool H. FULD.

REFERENCE

1 Chalmers, J. M. N., and Boheimer, K., *Lancet*, 1954, **2**, 920.

Measles

SIR,—In reply to Dr. J. F. Lund's letter (*Journal*, May 21, p. 1279) I should like to support the opinion of your leading article (*Journal*, April 23, p. 1018) that the prophylactic use of antibiotics in measles is wasteful and unnecessary, provided that any complications that arise are treated early and effectively.

During the recent epidemic I have attended 105 cases of measles. None of these has had routine prophylactic treatment. Two cases developed signs suggestive of early bronchopneumonia, but responded quickly to antibiotics and neither developed the full clinical picture of bronchopneumonia. There was one case of acute otitis media, which resolved rapidly and completely with antibiotic treatment, and two or three mild cases of otitis media, which did not require any specific therapy.

I would submit that, in this small series of cases, these children have been saved trauma, their attendants trouble, and the country about £50; and that none of them is any the worse off as a result.—I am, etc.,

High Wycombe. J. MCLUSKIE.

SIR,—I should like wholeheartedly to support Dr. John Fry's stand (*Journal*, June 4, p. 1389) against the indiscriminate prophylactic use of antibiotics in the treatment of measles. Surely we require a little common sense in this matter. The only two complications of importance which antibiotics can prevent are acute otitis media and acute chest infection. The acute stage of measles, when these complications are likely to occur, lasts only some three to four days. This necessitates at least two visits from the general practitioner, on each of which occasions adequate warning of the onset of these complications can be obtained by the examination of ear-drums and chest respectively. Furthermore, the mother can be warned to inform the doctor immediately should the child complain of earache or should the cough worsen, when a further examination can be made.

The first visit is usually requested when the rash appears. If I find any injection of the drums or any signs in the chest on this occasion, I put the child on to oral penicillin, although this is seldom necessary. My second visit is made on the third day, when the rash is at its height or already

beginning to fade, when the same procedure is repeated. Any infection arising on the second day, even if it has passed unrecognized by a forewarned mother, is unlikely to have reached very severe proportions by the third day, when antibiotic treatment can be still highly effective.

Certain children are probably predisposed to secondary infection by factors which we do not yet fully understand. Administration of antibiotics prophylactically to these individuals will do nothing to increase their resistance to such infection; in fact it is more likely to have the opposite action. There is then a danger of infection with resistant organisms which have been allowed to flourish, owing to elimination of their antibiotic-sensitive competitors. We should aim for early and effective antibiotic treatment of complications in measles and should not allow any relaxation of our vigilance over them from a false sense of security in antibiotic prophylaxis.

On one point I would disagree with Dr. Fry. I consider that every case of acute infective otitis media, no matter how mild, should be treated with antibiotics. Although a number of these cases will clear up without such treatment, it is impossible to differentiate those which will go on to suppuration, with all its possible dangerous complications, from those which will not. It is just these cases which require intensive antibiotic therapy, and the earlier it is given the better. This also applies to the treatment of the inflamed throat when the infection is other than catarrhal. To withhold antibiotic therapy from a case of streptococcal tonsillitis, even if this infecting agent is only suspected, is to court the risk, however slight, of serious complications such as acute nephritis and acute rheumatism. There would seem to be no contraindication to the widespread use of oral penicillin for this purpose, as there have been no reports of any fatal reactions to penicillin by this route, such as have occurred, albeit rarely, after intramuscular injection.—I am, etc.,

Twickenham, Middlesex. DAVID WHEATLEY.

Drug Eruption from Carbromal

SIR,—Our attention has been drawn to the article entitled "A Purpuric Drug Eruption Caused by Carbromal," by Dr. Peter Borrie (*Journal*, March 12, p. 645). In opening this article the author states that carbromal is closely related chemically to chloral. This might be taken to imply that it may therefore have some similar effects. Carbromal cannot possibly be described correctly as closely related chemically to chloral. The chemical relationship of these compounds gives no grounds, therefore, for expecting similar physiological action.—I am, etc.,

W. M. WOLF,
Director,
Darlington. Chemical Compounds Ltd.

Varicella with Neurological Complications in an Adult

SIR,—Dr. M. S. Pathy's case report (*Journal*, May 28, p. 1324) of a patient under the above title recalls a similar experience of my own early last year.

A man of 43 (also a bank cashier) contracted varicella from his wife and daughter on January 8, 1954. Their attacks were both very mild, but he had a most severe haemorrhagic confluent rash, and developed a bronchopneumonia, with headache, weakness of arms and legs, and intense toxaemia. He was transferred to hospital on January 15. By that time he was almost comatose and incontinent—temperature 101° F. (38.3° C.). There was slight nuchal rigidity; knee and ankle jerks were absent, but arm tendon reflexes were normal. He was too ill for cerebrospinal fluid to be taken, but a virus pneumonia and encephalitis were diagnosed, and he was given 1 million units of penicillin four-hourly, and chloramphenicol, 2 capsules four-hourly. Two days later chlortetracycline 1 capsule four-hourly was substituted for the chloramphenicol, but penicillin was continued until January 21. He also received 50 mg. ascorbic acid three times a day, and "ribothiron" 2 dr. (7.8 g.) every four hours from January 20 owing to a severe hypochromic anaemia (R.B.C. 3,000,000, Hb 52%, W.B.C. 10,700—polymorphs 91%, lymphocytes 5.5%, eosinophils 0.5%, monocytes 2%). For insomnia and restlessness he received 5 ml. paraldehyde intramuscularly.

By January 29 he was able to speak and incontinence had ceased; speech was slow and laboured, and there was delayed cerebration. He made a slow recovery, but was able to return home on March 7. He now exhibited a spasticity of both legs, which gradually recovered to a great extent, and a bilateral inferior hemianopia, with central sparing, making it impossible for him to read or to add up figures. The anaemia yielded to "ribothiron," and his haemoglobin, which rose to 79% before discharge, was 95% in March, 1955. He now has still much exaggerated knee-jerks but no clonus; the fields of vision have not improved. He has had to relinquish his banking career, but is able, with his wife's help, to conduct a small business. His power of concentration, however, is still poor, as is his memory.

I am grateful to Dr. John Mills for treating him in hospital, and to Dr. Graveson and Mr. F. Heckford for their assistance and advice in treatment of his neurological and eye symptoms respectively.—I am, etc.,

Ryde, I.W. L. FIRMAN-EDWARDS.

Professional Secrecy

SIR,—Dr. Robert Forbes (*Journal*, May 28, p. 1339) has criticized the new instruction on carnal knowledge of certified defective girls (H.M.(55)46), and, on the face of things, there must be support for the complaint in his last paragraph. It would have shown a fuller appreciation of all the aspects of the problem, and a suitable courtesy to those who guard the ethical standards of the profession, if at least some communication on the proposal had been made.

But reflection shows that the problem is not quite simple. Whatever may be the strict position in law or in medical ethics, the medical superintendent is not only the doctor who has medical care of the defective whose order has sent her to his hospital. He is also very much *in loco parentis*, as the patients themselves so often admit. They are very defenceless and very much children, and he must protect them in every necessary way. Again, there is no legal sanction at all for this, but it is necessary for the good of the service and the ultimate benefit of all patients that he should run his hospital so that it is recognized as giving a fair and honest as well as kindly deal to those entrusted to it.

Many years ago I was worried about a related problem and put it to a friend of much experience with the question, "Am I my brother's keeper?" The immediate reply was, "I'm afraid you are in this case," and I knew it was true. From this broader point of view, I think the medical superintendent must protect the particular patient, and, through her, all others who may suffer like trouble, by giving the police the chance to take action if there is a good case. Whether this is done indirectly through the Board of Control or directly by report to the police may not really be so very different a matter.—I am, etc.,

Wimbledon. NOEL H. M. BURKE.

Anxiety Neurosis

SIR,—May I comment on one aspect of Dr. Ronald A. B. Rorie's excellent article (*Journal*, April 30, p. 1062) on "Anxiety Neurosis: Treatment by the General Practitioner"? Dr. Rorie describes the melancholy process by which the patient attends several specialists, the diagnosis being made "in a negative manner, by exclusion of organic disorder, rather than in a positive recognition of the various neurotic syndromes." While it is clear that prolonged investigations, which themselves cause worry and eventually trail away into a dismal anticlimax of phenobarbitone, are undesirable, it is even more harmful to ascribe early organic disorders to neurosis. The diagnosis is not always easy, and this way the major tragedy lies.

Further, to convince the modern anxious patient of the nature of his symptoms—and he is to-day rather sophisticated about *x* rays and the like—may require a negative barium meal, chest *x*-ray, blood count, and so on. Indeed, such investigations are often most desirable if the physician is to exclude organic diseases. How, then, can we avoid the pitfall of endless specialists?

In most cases the general practitioner quickly realizes the probability of functional aetiology; often his past

knowledge of the patient and family serves him here. Special investigations may be required. Now if the practitioner can arrange these himself directly with the appropriate pathological or radiological department, then he can explain the purpose of the tests to be done and their probable negative result, and throughout the investigation he, the G.P., remains the doctor in charge of the case. His patient's confidence in him is enhanced, and his explanations, advice, and reassurance are well received by a receptive, co-operative individual. It is therefore perhaps appropriate to end with a plea to the hospital authorities to make direct access to diagnostic facilities universally available, and to general practitioners to use them.—I am, etc.,

London, E.6. DAVID H. LEWIS.

Dermatomyositis

SIR,—A recent personal study[1] of nine cases and a review of the literature of dermatomyositis has convinced me that this diagnosis covers at least three separate entities which can be distinguished on natural history and clinical features rather than biopsy findings.

(1) *Chronic progressive dermatomyositis* (Petges and Cléjat)[2]: This, the true pattern of dermatomyositis, may present acutely in children, but more commonly an insidious onset leads to irreversible changes before it is clearly recognized. Early features include low-grade fever and tachycardia, erythema and scaling mainly of exposed surfaces, transient oedema, particularly of the orbits; and periarticular pain and tenderness from involvement of tendons. Later tender muscles undergo a slow inexorable progression to generalized atrophy, woody fibrosis, and contractures with grotesque deformities. In parallel the affected skin develops changes of the poikiloderma atrophicans vasculare type with leashes of telangiectasia especially of the eyelids and sternum. A peculiarly expressionless alabaster facies is common, later becoming almost cadaveric. Other inevitable features are the Raynaud phenomenon with secondary sclerodactylia and calcinosis, diffuse or as localized peritendinous nodules. Renal involvement does not occur, but polyserositis, splenomegaly, and involvement of the bowel wall may be seen. In more than one typically deformed patient evidence of pulmonary hypertension and right heart failure has appeared, and has been shown[3] by exclusion to be due to an obliterative process in the smaller pulmonary arteries. Long-term prognosis is poor, and A.C.T.H. or cortisone therapy seems only to give temporary symptomatic improvement without halting this progress of reparative fibrosis. Very rarely in these cases one sees the hide-binding of scleroderma, a variable cutaneous symptom of, and not a synonym for, progressive systemic sclerosis of which this type of dermatomyositis is probably a variant.

(2) *A symptom complex associated with coincident visceral neoplasm*: Since Bezecny's[4] paper in 1935 there have been over 50 recorded examples in the relevant age group of the association of a relatively acute dermatomyositis with neoplasm of any organ or tissue, including Hodgkin's disease and other reticuloses. Two of my cases had bronchogenic carcinoma, one an oesophageal neoplasm. The skin lesions may resemble closely a disseminated lupus erythematosus in appearance and distribution, and atrophic weakness rather than tenderness is shown by the muscles, which tend to be those of the girdles and proximal limb groups. Associated visceral lesions can be attributed to the neoplasm or metastases. An awareness of this association, together with the fact of reported instances of recovery with successful treatment of the neoplasm, demands exhaustive visceral investigation of cases of dermatomyositis in this age group.

(3) *A polymyositic form of polyarteritis nodosa*: Typically this is a hyperacute, fulminating, or self-limiting condition, commonest in young adults, which quickly follows a recognized infection with or without treatment with sulphonamides, etc. Extreme early malaise, high fever, and disproportionate tachycardia are usual. A general distribution and extraordinary pleomorphism characterize the skin lesions, which vary from erythema fugax, multiforme, or nodosum to livedo reticularis and haemorrhagic necrotic or gangrenous lesions. Painful and tender swellings occur and, if periarticular, make distinction difficult from acute polyarthritis, which occurs in some cases. Oedema is excessive but limited to the area of affected muscles or to the orbits, where the combination with erythema gives a heliotrope bloating which has been likened to cadaveric decomposition. Generalized oedema suggests renal damage or cardiac failure. Muscle involvement is generalized, causing exquisite pain on movement and marked tenderness and swelling. Polyneuritis may cause some of the ensuing weakness and wasting, which are, however, reversible. Ischaemia or infarction may affect any organ, and renal lesions commonly lead to hypertension and uraemia. Polyserositis, hepatomegaly with jaundice, splenic enlargement or infarction, and retinal lesions have been described. A high E.S.R. and a high polymorphonuclear leucocytosis are the rule—one of my cases had a W.B.C. total of 125,000/c.mm. without significant eosinophilia. Creatinuria is also excessive—1,000–2,000 mg. per day.

These cases are an urgent indication for the asbestos cover of A.C.T.H. or cortisone, and, as in systemic lupus erythematosus, the daily controlling dosage may initially be 150 mg. or more of A.C.T.H., or equivalent amount of cortisone, with slow reduction to prevent escape.

Dr. Hillas Smith[5] has clearly described a case of this last type with, *inter alia*, an episode of bowel or mesenteric infarction and severe renal damage. I would plead that future authors should attempt—if only in retrospect—to classify their cases into these divisions which have, too, important therapeutic implications.—I am, etc.,

Aberdeen. IAN W. CALDWELL.

REFERENCES

1 Part 2 M.D. Thesis, 1954, Aberdeen University.
2 *Ann. Derm. Syph. (Paris)*, 1906, **7**, 550.
3 *Brit. Heart J.*, in press.
4 *Arch. Derm. Syph. (Wien)*, 1935, **171**, 242.
5 *British Medical Journal*, 1955, **1**, 770.

Mistaken Capsules

SIR,—The recent correspondence on the treatment of barbiturate intoxication prompts me to call attention to a cause of accidental barbiturate overdosage which I have not previously seen reported—the taking of "carbrital" capsules by mistake for "chloromycetin." The mistake is readily made, and two cases have been seen in this hospital.

The first occurred when a house-physician with a severe upper respiratory infection wished to treat herself with chloromycetin and helped herself from the ward stock. When she recovered consciousness she realized that she had taken capsules of carbrital in error. The second case was that of a woman with acute sinusitis for whom capsules of chloromycetin were prescribed by her doctor. After 24 hours of the treatment she became unconscious and was admitted to hospital, where marked drowsiness and nystagmus were the only abnormal signs. The cerebrospinal fluid was normal and the patient recovered spontaneously overnight. When she came to herself she was shown capsules of carbrital and capsules of chloromycetin, and unhesitatingly identified the former as those which she had been taking before she lost consciousness.

Carbrital contains pentobarbitone 1½ gr. (0.1 g.) and carbromal 4 gr. (0.26 g.) in a white capsule marked by a single navy-blue band. Chloromycetin is put up in a slightly smaller white capsule marked with a grey band. In a poor light the colours of the bands are not readily distinguishable. These cases show how easily confusion may occur and suggest that some more obvious distinguishing mark should be applied to the capsules, which are both marketed by the same firm.

I am grateful to Sister M. A. Woodman, who first made me aware of this problem, and to Dr. T. H. Boon for permission to report the two cases.—I am, etc.,

Newcastle-upon-Tyne. R. E. IRVINE.

Care of McGill Tubes

SIR,—Complaints have been made from time to time about the poor attention given in operating theatres to the sterility of anaesthetist's appliances—for example, McGill tubes—but from the medico-legal report in the *Journal* of May 28 (p. 1347) it would appear that the pendulum has swung, and that these tubes are now being autoclaved. It is to be hoped that this practice will not spread, for many of the tubes now supplied are already of hard rubber with chisel-like ends, well calculated to do damage in the nose (false passages have been reported). I would suggest that McGill tubes must never be autoclaved, but that they should be well boiled to ensure that they are soft.—I am, etc.,

London, N.W.8. R. J. CLAUSEN.

The Ban on Heroin

SIR,—May I add my protest against the intended ban of the manufacture of heroin? No drug gives such relief as does heroin in the advanced stages of tuberculosis both for the incessant cough and for the equally troublesome gastric symptoms. If our legislators inquire more fully into the merits of the drug they must be convinced of the foolishness of their ill-advised ban.—I am, etc.,

Birmingham, 33. W. H. OSBORN.

Coat the Pill

SIR,—With the manufacturers of proprietary medicines constantly on the look-out for new preparations and new forms of old ones, may I, through your *Journal*, draw their attention to the need for a more palatable form of such antimalarial drugs as mepacrine and proguanil? These are notoriously bitter in taste, and I have known several children absolutely refuse to take their daily paludrine whichever way it has been served. I think this difficulty would easily be overcome if these tablets were sugar-coated.—I am, etc.,

Enugu, Nigeria. F. M. OWERS.

Lumbago

SIR,—Mr. V. B. Green-Armytage asks (*Journal*, May 28, p. 1341) why men get lumbago so much more often than women—an observation that certainly tallies with my own experience. The reason appears simply that men lift heavy weights and thus, by attrition and compression, crack the annulus. Sudden subluxation of this loose fragment is then apt to cause lumbago—a recurrent phenomenon as in internal derangement at other joints.

Women, by contrast, do much stooping, which, in the course of years, causes a gradual retropulsion, leading to intermittent backache coming on after keeping the back bent for some time. Later, permanent backache from a small constant protrusion may result. In my view the different behaviour of the disk in the two sexes merely reflects the difference in the work men and women normally perform.—I am, etc.,

London, W.1. JAMES CYRIAX.

Gorleston Holiday Camp for the Handicapped

SIR,—The above camp is to be held again this year in the last two weeks of September. There is already a waiting-list for both weeks, so it is obvious that the camp fulfils a long-felt want amongst disabled people.

I should like to ask for the co-operation of the family doctors of those who are going to attend the camp in sending me as full particulars as possible on the confidential form which each handicapped applicant has received. It is quite a serious undertaking to care for a large group of severely handicapped people, and any information about their medical condition and usual treatment would be invaluable to the local general practitioner who acts as medical officer to the camp. A clear statement of the exact nature of the handicap will also be most helpful to the organizers, who have to allocate sleeping accommodation and arrange for voluntary help.

Any members of the British Medical Association who may be on holiday in the neighbourhood would be welcome visitors to the camp.—I am, etc.,

Norwich. IRENE B. M. GREEN,
Vice-chairman, Norfolk Voluntary Association for the Welfare of the Physically Handicapped.

POINTS FROM LETTERS

Hot-water Bottles

Mr. M. J. HORGAN (Tralee, Co. Kerry) writes: The hot-water bottle is a dangerous convenience. . . . To the infant, aged, and anaesthetized it is a burning problem. It suffers sporadically and surprisingly from enuresis. Thirdly, and possibly uniquely, it has now been convicted of bony injury. I was recently consulted by a lady who told me that, lying half awake, she noticed something strange about her little toe. She made a quick movement with her leg which provoked excruciating pain in her little toe. She had insinuated it into the hole in the stopper of the bottle and the sharp movement had fractured the basal phalanx. Subsequent radiological examination showed a spiral fracture of the middle of the proximal phalanx. I make no claim to originality in this description. Presumably if others have encountered the condition they will let us know of it. In the meantime I should like to feel that I have described my only original syndrome. I shall christen it "hot-water bottle toe," or, perhaps more simply, "Horgan-toe."

Papilloma of the Bladder

Dr. C. HORWITZ (London, N.1) writes: I am wondering whether the following case constitutes a record in the number of diathermies for recurrent papilloma of the bladder? A man aged 56 years employed as a printing manager has been under my care since 1947 for recurrent papilloma of his bladder. He has been admitted to hospital on 29 occasions and on each he was found to be suffering from a recurrence. The last time he was admitted to hospital was on April 24 when for the first time he was found to be free from papilloma of his bladder. He is to be readmitted in three months' time for observation.

An Occupational Hazard

Dr. R. BAUER (Cardiff) writes: I should like to point out that the injury as described by Dr. Edith Faulkner (*Journal*, May 7, p. 1158) closely resembles those incurred by pig-slaughtermen, and known on the Continent as "pig-stabber's injury." The injured part is generally the femoral vein, and the fatal outcome caused by air embolism. In these cases if the injured man was not brought to hospital with his hip maximally bent, but with the leg stretched, the vein was kept open and air was aspirated.

The Changing Face of Medicine

Dr. W. F. BENSTED-SMITH (Newton Ferrers) writes: As a tail-piece to Mr. Clifford Kennedy's article on the changing face of medicine (*Journal*, April 30, p. 1045), might I suggest that if "the State" had to pay the costs of both sides in lost free legal aid cases a way would soon be found to thin out the number of such cases brought to court?

A Convenient Measure

Dr. MARY G. H. EDWARDS (New Milton) writes: I have always found it tiresome, especially when short of time, to measure the distance of the apex beat of the heart from the midline of the sternum. Tape-measures tend to fall off one's knee and the figures are not easy to see in a bad light at night. I have therefore adopted a simple, time-saving method. Adhesive strapping, one inch (2.5 cm.) wide, is stuck on the tubing of the stethoscope, covering alternate inches. Three bands, so placed, enable one to measure 5 inches (12.7 cm.). The stethoscope is always there. The marks are visible by any light and not a second is wasted.

Hospital Improvements

Miss OLIVE MATTHEWS (Coaley, Glos) writes: In response to my offer (*Journal*, May 14, p. 1223) to give away *Hospital Improvements*—how to improve the daily life of the patient in the ward—I am pleased to say that 28 doctors have written to ask for it (duly enclosing fourpence to cover cost of postage and envelope). I would like to ask the recipients to send me their comments, and especially any constructive criticism.

Obituary

JOHN EVERIDGE, O.B.E., F.R.C.S.

Mr. John Everidge, consulting urological surgeon to King's College Hospital, died at his home in London on June 8. He was 71 years of age.

John Everidge was educated at King's College School and in the medical faculty of King's College, London, where he was junior scholar in 1904, winning the Alfred Hughes prize for anatomy. At King's College Hospital he won the senior scholarship in 1907, and qualified M.R.C.S., L.R.C.P. in the following year. After holding the appointment of house-surgeon at King's College Hospital, he became Sambrooke surgical registrar and surgical tutor in 1912, the year in which he obtained the F.R.C.S. During the first world war he served with distinction in France as a surgical specialist, with the rank of major, being mentioned in dispatches and, at the end of the war, being appointed O.B.E. for his services. "The Major" was the nickname by which he was known to students for several decades.

Everidge returned to King's in 1919 as junior urological surgeon, becoming the senior surgeon in his department and lecturer on urology when the late Sir John Thomson-Walker retired in 1929. From then on he gave up general surgery, though he never lost his interest in it. His fame as a urological surgeon spread far beyond his own hospital, and he held numerous consultant appointments in and around London, including those of consultant to Queen Alexandra Military Hospital, Millbank, and to the London County Council. The author of numerous papers on his specialty, he contributed articles to Rose and Carless's *Textbook of Surgery* and to *Modern Operative Surgery*, and for some years he was chairman of the editorial committee of the *British Journal of Urology*. He was also a member of the council of the British Association of Urological Surgeons, and for some years the treasurer of that body. His slight deafness made him refuse the presidency, but he worked hard for urological interests throughout his career. At the Royal Society of Medicine he was president of the Section of Urology in 1939–40. During the second world war he was one of the senior staff at Horton Emergency Hospital, and at the end of the war, when he was due to retire from the staff of King's, he was appointed active consulting urological surgeon, and in 1953 the title of emeritus lecturer was conferred on him by the council of King's College Hospital Medical School in recognition of his long and valuable services to the school. Three years before this he had been made a Fellow of King's College.

In his younger days Everidge was an accomplished tennis player, being a member of King's "six" in 1906, and in later life he showed a similar aptitude for golf, which, with fishing, became his favourite recreations. He married Miss Kathleen I. Robertson and had one son and one daughter.

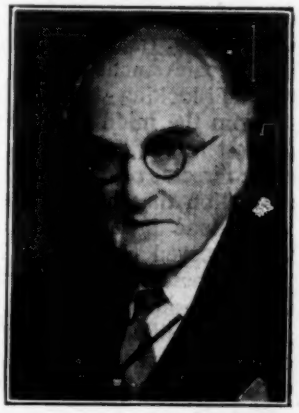
We are indebted to Mr. J. G. YATES-BELL for the following appreciation: John Everidge was one of England's leading urological surgeons. At King's his splendid teaching, imparted with wit without crudity, attracted large throngs to his clinics. In surgery he was a pioneer in transurethral prostatic surgery as long ago as 1927, and played a part in the development of the modern resectoscope. He was always helpful to his juniors, and it was a matter of pride that so many of his old house-surgeons held consultant posts. His personal charm was outstanding, and he was held in the highest esteem by his colleagues and friends; patients were devoted to him by virtue of his sympathy.

He had many interests outside his work, lawn tennis in his early days, and in more recent years golf at Epsom and Deal, while many week-ends were spent fishing with urologist friends. He was a member of the Flyfishers' Club.

He always remained young—in surgery by keeping up to date with new procedures, and in private life by his enjoyment of all student activities, dances, and fast cars. His after-dinner speeches were always polished and entertaining. He will be greatly missed as a surgeon and as a friend.

R. N. SALAMAN, M.D., F.R.S.

We record with regret the death on June 12 at his home at Barley, Hertfordshire, of Dr. Redcliffe Salaman at the age of 80. A scholar and research worker of great distinction, Redcliffe Nathan Salaman was for a short time director of the pathological institute at the London Hospital, but he soon turned towards genetic and agricultural research, and for the whole of his life had a host of other interests which brought him renown in many countries of the world.



[*Walter Stoneman*

We are indebted to Professor CHARLES SINGER for the following tribute: As I have known Redcliffe Salaman since childhood I venture to send you some account of this most remarkable man. His accomplishments are too varied for detailing here, but his distinguished career has points of medical interest, not least of which was his extraordinary success in combating his early disability. He was an unusually handsome man who, till a very few weeks ago, gave the impression of an alert, genial country gentleman, a lover of the open air, but also one with a wide knowledge and kindly estimate of men and of affairs. All these things he was, but he was much more. I wish that I could convey in words the impression of cheerful, breezy, combative, intelligent optimism that his presence exhaled.

He was a member of a Jewish family, the progenitors of which came to England from Holland in the mid-eighteenth century. Born in London in 1874, he was educated at St. Paul's School and at Trinity Hall, Cambridge, of which he was a scholar and later an Honorary Fellow. He took a first in the tripos and was much influenced by the physiologists Michael Foster and Gaskell, the anatomist Macalister, and the anthropologist Haddon, all of whom remained his friends throughout their lives. He entered the London Hospital as a student and found time for research even before becoming qualified in 1900. As house-physician to Henry Head, F.R.S., he was naturally drawn to experimental pathology, and spent the years 1901–2 in research on those lines at Würzburg and Berlin. On his return he became director of the pathological institute of the London Hospital and a little later pathologist to the Zoological Gardens. In these capacities he did much important work which he was actively publishing when,

in 1904, he developed pulmonary tuberculosis. He immediately entered a sanatorium in Switzerland, where he remained for eighteen months. On his return to England he decided to live in the rural surroundings of Barley, in Hertfordshire. He took there a house which remained his dwelling for the rest of his life. With due care his health steadily improved and he began the series of activities which, by their variety and the vigour with which they were prosecuted, made him a well-known and much-liked, if sometimes controversial, figure in widely different circles.

Undoubtedly his most important scientific work was on the genetics of the potato, on which he became the leading authority. He began his researches on this line in 1906 and continued them to the end of his life; his last paper on it appeared in the present year. It is characteristic of the man that he treated the subject on the very broadest lines, at once theoretical and practical, economic and physiological, literary and historical. His largest single contribution was the fascinating volume of 1949, *The History and Social Influence of the Potato*. Recognized as a classic from the day of publication, it is a most attractive storehouse of original research and observation, fresh in outlook and presentation. It is no small achievement to have made a moving romance of this dull-looking vegetable.

From the middle nineteen-twenties Salaman took an interest in the rising study of viruses. In 1926 he became director of the Cambridge Potato Research Station, a position that he occupied until 1939. The scientific work done in this and kindred capacities led to his well-deserved election as Fellow of the Royal Society in 1935, and to his chairmanship of the National Institute of Agricultural Botany in 1928 and later years. His greatest positive agricultural achievement was the introduction of potato strains with relative immunity to certain viruses and a high yield. Altogether he was the author of over fifty scientific papers on various aspects of the biology of the potato. This by no means exhausted his contributions to agricultural science. Thus he wrote on the inheritance of fur-types in rabbits (1922), and contributed to a Royal Society discussion on ultramicroscopic viruses in animals and plants (1929) and on the state of the "Theory of Natural Selection" (1936). Elsewhere he developed the themes of virus diseases in plants in general (1936) and on economic application of Mendelian methods (1936). He had also an intense interest in anthropological problems, and was the author of a whole series of works dealing largely with the physical anthropology of the Jewish people. Of special medical bearing were his views on the relation of the virus diseases of man and animals to those affecting plants in a communication to the *Lancet* (1937), and on deformities and mutilations of the face in ancient Peruvian pottery in the *Journal of the Anthropological Institute* (1939).

Salaman always devoted a large portion of his activity to public service. He became a J.P. for Hertfordshire in 1907 and was on the bench for 43 years, during 23 of which he was chairman of one of the divisions, member of the quarter sessions appeal court, and member of the county agricultural committee. He was also a Commissioner of Taxes. He combined all this with innumerable other public enterprises. He was almost from the beginning in 1933 a very efficient and attentive member and for long the treasurer of the council of the Society for the Protection of Science and Learning. This body seeks to maintain in active work scholars and scientists who are refugees from oppression of any sort, regardless of their race, religion, colour, or politics. Salaman's widely generous sympathies here found a very natural and useful outlet.

Something must be said on Salaman's special activities on behalf of the Jewish people, since his interest there, too, was specially in the encouragement of science and learning, and, not least, of higher health standards. He was president of the Jewish Historical Society (1920), and for the last forty years of his life was on the council of the Jews' College, a theological foundation. He was a founder of the Jewish Health Organization (1923), was largely responsible for the founding of a chair of Rabbinic studies at Cambridge (1925), and was a member of the board of governors of the Hebrew University of Jerusalem, which he visited many times and served in many capacities.

Salaman had a singularly happy domestic life. His first wife, Nina Davies, the daughter of a distinguished scholar, was a scholar and poetess in her own right. She was particularly successful in her translations of mediaeval Hebrew poetry and devotional literature, and many of her efforts have become standard. She was a lady of quite exceptional beauty, charm, and wisdom. She bore her husband five children, two of whom are medical men, and died in 1925. He was no less fortunate in his second union with Gertrude Lowy, who survives him.

JAMES HUDSON, M.D.

We record with regret the death on May 17 of Dr. James Hudson at his home at Watermillock, Penrith, Cumberland, at the age of 90. Dr. Hudson, who was in general practice at Newcastle-upon-Tyne for over fifty years until he retired in 1948, was a member of the Council of the British Medical Association for fourteen years and a past president of the North of England Branch.

James Hudson was born at Dumbarton on December 27, 1864, and studied medicine at Glasgow University, where he graduated M.B., C.M. in 1889, proceeding to the M.D. five years later. He first entered general practice as an assistant in a mining district in Lanarkshire, and for a time acted also as senior assistant medical officer to the Coltness Iron Company. In 1893 he settled at Newcastle-upon-Tyne and remained in practice there until 1948, when he retired to Watermillock.

Hudson, a man of boundless energy, always took an active interest in professional affairs, and by regularly attending medical meetings and lectures he kept himself well informed about current medical thought. He was honorary secretary of the Newcastle-upon-Tyne Division of the B.M.A. from 1915 to 1921 and chairman from 1915 to 1918, and president of the North of England Branch in 1925–6. From 1925 to 1938 he represented the Branch on the Council of the Association, and from 1928 to 1940 he was a member of the Central Ethical Committee. He also represented his constituency at eleven Annual Representative Meetings from 1921 to 1939. When the B.M.A. held its Annual Meeting at Newcastle-upon-Tyne in 1921 he acted as one of the honorary secretaries of the Section of Venereal Diseases, and in the following year at Glasgow he served as a vice-president of the Section of Medical Sociology. He was chairman of the local medical war committee throughout both the first and second world wars. He was also a life member and a past president of the Newcastle Medical Society and a past president and

treasurer of the North of England Glasgow University Club. He is survived by one daughter, Mrs. Hudson having died last year.

Dr. GEO. P. HARLAN writes: Much regret will be felt by very many people, both medical and lay, at the death of Dr. James Hudson. He retired to Watermillock after a long, useful, and active life spent in practice at Newcastle-upon-Tyne. He often told me of his experiences as an assistant in Lanarkshire, where, before the days of cars, he made his calls on horseback, then a previously untried form of transport for him. While he was in this assistantship he had to help to deal with a severe epidemic of typhoid fever. On another occasion a mother told him that all her children died in the first few weeks of life. He felt very sceptical of the mother's statement, having just delivered her of a fine healthy child, but after a time the apparently healthy infant developed spasms and died. The condition was diagnosed as tetanus, and infection had arisen from infected water drawn from a barrel which stood outside the door, the water having been used to bath the child and infection having occurred through the umbilicus. James Hudson did not agree with the panel system introduced under the National Insurance Act of 1911 and so remained in private practice, and he adopted the same attitude when the National Health Service came into operation in 1948. I appreciated very much his friendship, as he was an excellent example for a young man. He was of the finest type of general practitioner, for he was not only the doctor but also the friend of the family, and he has left behind him a reputation of which anyone might be proud. Many of his old patients still remember him and all he meant to them. In 1948 he retired to Watermillock to enjoy a well-earned rest. With his inherent enthusiasm and energy, however, he could not be idle, and so he identified himself with the affairs of the village, becoming one of its leaders. Certainly he will be very much missed by all the inhabitants. It is good to think that after his long and busy life at Newcastle-upon-Tyne he was able to exercise his many gifts for the welfare of others at Watermillock.

R. A. LYSTER, M.D., B.Sc., D.P.H.

Dr. R. A. Lyster, formerly county medical officer for Hampshire, died at his home at Bournemouth on June 3 aged 82.

Robert Arthur Lyster was educated at King Edward's School, Birmingham, and at Queen's College and Mason University College in the same city. He took the B.Sc. of London in 1893, and with the help of scholarships and exhibitions he went on to study medicine at Birmingham University, qualifying in 1900. Having determined on a career in public health, he continued to study bacteriology, chemistry, and hygiene as a post-graduate, taking the D.P.H. in 1901, the degrees of M.B., B.Ch. in 1902, and the B.Sc. (public health) in 1905, and proceeding M.D. in 1908. One of his first public appointments was as bacteriologist to the West Riding County Council, but in 1906 he returned to Birmingham as medical officer of health for the Handsworth Urban District. During these years he was lecturer in public health and forensic medicine to the University of Birmingham, but he had to give up this teaching work shortly after his appointment in 1908 as county medical officer, chief school medical officer, and chief tuberculosis officer for Hampshire. He retained this post until his retirement in 1929. During his years in Winchester he saw great changes in the public health service, and in particular he will be remembered for his efforts to extend the facilities available for the treatment of tuberculosis.

Lyster's enthusiasm for preventive medicine won him renown all over Britain. He was editor of the journal *Public Health* from 1918 to 1925, and president of the Society of Medical Officers of Health during 1925–6 and of the Association of County Medical Officers of Health during 1926–7. An examiner in public health to several universities, he taught the subject himself at St. Bartholomew's Hospital and was a member of the faculty of medicine and board of studies in hygiene in the University of London. He also served on numerous advisory committees to Government departments, was a member of the Central Midwives Board from 1921 to 1930, and was sent as a delegate from this country to several international conferences. During the first world war he served in the R.A.M.C. as a specialist sanitary officer in the Winchester area.

Before he resigned from the public health service Lyster served on several B.M.A. committees, including the Public Health Committee, and was a member of Council from 1925 to 1927. In the years before the first world war he had attended several Annual Meetings as a Representative of his Division. In 1928 he was adopted as Parliamentary Labour candidate for Winchester, but he was unsuccessful in the elections of 1929 and 1931. He was also unsuccessful as the Labour candidate for Preston in 1935. After his retirement from the post of county medical officer of Hampshire in 1929 he went to live in Bournemouth, where he was a very active member of the town council for many years, serving as chairman of the general purposes committee.

E. C. CLEMENTS, C.B.E., M.R.C.S.

Group Captain E. C. Clements, formerly consultant in ophthalmology to the Royal Air Force, died at Horsmonden, Kent, on May 19, at the age of 81.

Edward Cecil Clements, who was born on April 20, 1874, received his medical education at the Middlesex Hospital, qualifying M.R.C.S., L.R.C.P. in 1901. He then studied ophthalmology at Moorfields, and later was engaged in ophthalmic practice at Lincoln. Appointed to a commission in the R.A.M.C. (T.A.) in 1908, he was mobilized on August 5, 1914, for service in the first world war, during which he served with the Royal Flying Corps. Later he was seconded to the Royal Air Force as an eye specialist.

He soon found in pilots the same tendency to lose the power to maintain binocular single vision as he had observed in civilian practice in bank clerks and technicians using precision instruments. Recognizing the importance of such a defect on the judgment of distance when landing aircraft, he set up in July, 1918, at the Hampstead Aviation Candidates Medical Board what is believed to have been the first school for the treatment of heterophoria in London, making use of the then recently invented Maddox rods for diagnosis and Black's amblyoscope for treatment.

In 1919 Clements was appointed to a permanent commission in the Medical Branch of the Royal Air Force in the rank of squadron leader. He was promoted wing commander a year later and group captain in 1928. Employed in his specialty throughout his service, he became consultant in ophthalmology in 1931. He was appointed O.B.E. in 1919 and promoted to C.B.E. in 1934, the year in which he retired.

Although his standards for acceptance for aircrew have been criticized as being too rigid, there can be no doubt that the orthoptic training instituted by Clements increased the confidence and reduced the wastage of pilots undergoing training. His pioneer work holds an honoured place in the records of aviation ophthalmology.

D. Y. SOLANDT, M.D., Ph.D., F.R.S.C.

Dr. Donald Young Solandt, who died in Toronto on March 30 at the age of 48, was professor and head of the department of physiological hygiene and professor of physiology, University of Toronto. An outstanding authority on the biophysical aspects of physiology, he made a special study of muscles, of the special senses, and of environmental conditions. His publications appeared in many medical and biophysical journals, and he was author of a textbook entitled *Highways to Health*.

Donald Solandt was born in Ottawa, Ontario, and entered the University of Toronto in 1925, remaining closely associated with the university until his death. He was a brilliant undergraduate, and his work gave promise of future achievements. He graduated in medicine in 1933, and his interests then led him to post-graduate research in the University of Pennsylvania and later in Britain. In 1936 he obtained his Ph.D. degree from the University of London and returned to Toronto to assume his duties in the department of physiology, where he was in charge of biophysical research. He retained his professorship in this department when, in 1941, he was appointed professor and head of the department of physiological hygiene. During 1941–5 he was on active duty with the Royal Canadian Navy as surgeon commander in the Medical Research Division. In recognition of his contribution to the protection of night vision he was awarded, in 1947, the Medal of Freedom with Bronze Palm by the U.S. Government.

Many committees of the National Research Council of Canada benefited from Dr. Solandt's active interest. He also served on the Advisory Committee of the Department of National Health (Canada) and on committees of the American Public Health Association. He was a member of several scientific societies in Britain, Canada, and the United States and was an honorary fellow of the American Medical Association.

A loyal friend, Solandt was held in high esteem by all who knew him. His great store of knowledge in many fields made him a stimulating companion. He will be remembered for his keenness and adaptability of mind and his never-failing courage in the ill-health which sapped his energy in his early undergraduate days and throughout the rest of his life. He is survived by his widow, formerly Barbara Garrard, of London, and three daughters.

Professor RONAN O'RAHILLY writes from Wayne University, Detroit: As a former student, demonstrator, and friend of the late Professor D. T. BARRY (whose obituary was published on May 7, p. 1161), I would like to contribute my personal appreciation. In his long research career he was probably best known in the field of cardiac perfusion, and it was my good fortune to assist him in many experiments. He possessed an indefatigable enthusiasm for physiology and contributed numerous publications to a wide variety of scientific journals. In London, more than a dozen years after his retirement, he was still interested in receiving reprints. In his younger years he was a skilful exponent of chess, bridge, squash, and golf. He had a keen sense of humour, and to a student who informed him during an oral examination that she passed 1,500 litres of urine daily he merely remarked, "How very awkward!" Although students were sometimes awestruck in his presence, he was a very stimulating confrère to those who were fortunate enough to know him outside of the classroom. To these his friends, as to the long line of students who learned in his laboratory, his passing will be a sincerely felt loss.

Dr. B. HIRSH writes: I was deeply moved to read in the *Journal* of June 4 (p. 1393) that Dr. W. J. GRANT, of Shrewsbury, had passed away. I referred to his inspiring leadership in a speech at the recent Annual Representative Meeting. It is tragic for me to think that while I was referring to him he was already dead. Allow me to pay tribute to a great fighter—in the face of tremendous odds—against what we considered to be injustice.

Medical Notes in Parliament

Safety and Welfare Legislation

The Queen's Speech, with which the new Parliament was opened on June 9, promised active promotion of the development of nuclear energy for peaceful purposes, and legislation to safeguard the health and provide for the safety and welfare of those employed in agriculture and industry, and to reduce the pollution of the air by smoke and other causes.

Mr. ATTLEE, Leader of the Opposition, commenting on the health legislation, described it as an extraordinarily meagre instalment of the recommendations of the Gowers Report. The Trades Union Congress had been in consultation with Ministers for a long time, and had been led to believe that a far more comprehensive measure would be introduced to deal with office workers and non-industrial employees, who were totally unprotected.

Sir ANTHONY EDEN, the Prime Minister, explained that there had been a considerable increase in accidents in agriculture and forestry. This was due to the introduction of machinery on a scale unparalleled anywhere in the world. This country had the most highly mechanized agriculture there was. It therefore seemed necessary to the Government to start with this particular measure. But that did not mean that they proposed to stop there. They had considered whether proposals for the railways might be included, but as it was not certain that it would be possible to get the necessary separate Bill through in this session it was thought wiser not to include it in the programme.

The Ban on Heroin

Two Ministers were questioned on June 13 about the ban on the manufacture of heroin. Mr. SOMERVILLE HASTINGS (Barking, Lab.) and Mr. NIALL MACPHERSON (Dumfries, Nat. Lib. and Con.) asked the Minister of Health on what evidence the department held that there was an efficient substitute for heroin in the treatment of disease; what consultation he had had with medical practitioners before deciding not to license its manufacture; and on what grounds he took his decision.

Mr. IAIN MACLEOD said that the British Pharmacopoeia Commission were of the view in 1950 that a suitable alternative existed, and deleted the monograph on the drug from the 1953 edition of the *British Pharmacopoeia*. His Standing Medical Advisory Committee were specially consulted and entirely endorsed this view. As a result he advised the Home Secretary that there was no obstacle from this standpoint to his responding to the appeals of the World Health Assembly and the Economic and Social Council to prohibit the manufacture of the drug.

Mr. HASTINGS asked if there was any evidence of addiction in Britain, and whether the Minister had ever had, as he had had, an intractable cough which nothing but heroin would relieve. Mr. MACLEOD said that the answer, happily, was "No." There were people who believed that for a limited range of afflictions there was no true substitute for heroin. That had to be weighed against the larger claims of the Government playing their part in combating something which was a substantial social evil throughout the world. Although there might be little evidence of addiction in Britain it was entirely desirable that if they could get international agreement they should prohibit the manufacture of the drug everywhere.

Dr. EDITH SUMMERSKILL (Warrington, Lab.) asked whether the substitute was as effective as and much cheaper than heroin. Mr. MACLEOD said that was in dispute, but most people would agree with her. Mr. MACPHERSON asked whether supplies could not be made available to practitioners in those cases where it could be shown there was no adequate substitute, and whether, if he produced evidence of such cases, the Minister would consider it. Mr. MACLEOD said "Yes." The Home Secretary was going to receive a deputation from the British Medical Association, and these matters could be examined then.

Mr. WALTER ELLIOT (Glasgow, Kelvingrove, Con.) said that the drug was of great use in certain cases and could not be dispensed with. He urged the Minister to bend his utmost efforts to see that supplies were made available to reputable practitioners, as had been done before with many drugs as dangerous as this one. Mr. MACLEOD said that he would take that into account. All he could do was to take the best advice available: that was from his Medical Advisory Committee, which included the Presidents of the Royal Colleges, the Chairman of the Council of the B.M.A., and the President of the General Medical Council. Their view was one to which the greatest attention had to be given.

Deputation to Home Secretary

Sir ROBERT BOOTHBY (Aberdeenshire, East, Con.) asked the Home Secretary whether, in view of the protests of the British Medical Association and of the medical profession throughout the country against the threatened withdrawal of heroin, he would permit the manufacture of the drug in limited quantities for use by medical practitioners, and subject to a ban on its export. Sir HUGH LUCAS-TOOTH, Under Secretary, stated that the Council of the B.M.A. had asked the Home Secretary to receive a deputation on this subject, and he had agreed to do so.

Sir ROBERT BOOTHBY asked that the Home Secretary should bear in mind that, in the opinion of the majority of the medical profession, this drug alone could bring relief to certain types of pain, particularly connected with inoperable cancer. As there were only 40 heroin addicts known in this country, would he bear in mind that it was most undesirable that avoidable suffering should be inflicted on thousands of cases if adequate control of the drug could be devised? Sir HUGH LUCAS-TOOTH said the Home Secretary would prefer to discuss the matter with the deputation first.

Poliomyelitis Vaccine

Dr. BARNET STROSS (Stoke-on-Trent, Central, Lab.) asked the Minister of Health when it was proposed to vaccinate groups of children in Britain against poliomyelitis; and what type of vaccine was to be used. Mr. MACLEOD replied that a member of the staff of the Medical Research Council had just returned from a visit to the United States, where he had been studying the latest developments. His report was at present being considered. He expected to make a fuller statement to the House at an early opportunity. Dr. STROSS asked whether some of the tragic results of the use of the Salk vaccine in the United States had been due to the fact that the virus had not been completely killed. If it was used here, would the greatest care be taken to ensure that no such accident occurred? Mr. MACLEOD replied that it seemed probable that the explanation of the Cutter vaccine incident had been that it contained live virus. The Ministry of Health would be content only with the highest standards before they went ahead here.

Cost of Drugs Inquiry

Mr. A. BLENKINSOP (Newcastle-upon-Tyne, East, Lab.) asked the Minister what further progress had been made in discussions with the pharmaceutical industry regarding the cost of drugs and appliances prescribed through the Health Service. Mr. MACLEOD stated that the manufacturers both of standard drugs and of the main types of surgical dressings had been informed that the results of the cost investigations did not suggest there was any call at present for intervention by the Government, subject in the latter case to certain assurances. As regards the prices of proprietary preparations, since the special provisional reductions which were mentioned on January 31 discussions had been continuing with the industry on the general principles to be followed. Basic drugs, which could not be dealt with separately, were still under investigation, and meantime the firms themselves had continued to reduce the prices of some important drugs. Mr. BLENKINSOP asked if the Minister could give any indication when the discussions would end. Mr. MACLEOD said that he did not particularly envisage them coming to an end at all. It seemed to be a continuing pressure that ought to be kept up over a long period. He added that he thought it would be possible to keep effective and reasonable control over the costs, but there were very considerable problems to reconcile with the need for economy.

Antibiotics

Dr. BARNET STROSS asked the Minister of Health what was the extent of the emergence of strains of diseases now resistant to the common antibiotics such as penicillin, and what was the extent to which uncontrollable allergies to penicillin were appearing. Miss PAT HORNSBY-SMITH, the Parliamentary Secretary, said the Minister was advised that it had been established that strains resistant to penicillin, and in varying degree to certain other antibiotics, were emerging, and that allergies to penicillin were appearing, although it was not yet certain how far any of these was uncontrollable. The Minister was not at present competent to give any more detailed figures or particulars in these matters.

Regional Board Audit Staff.—In answer to a question the Minister of Health said that the staff employed in the audit of the accounts of all National Health Service hospital authorities, executive councils, and certain other authorities conforms with comparable audit services in the Civil Service, where a professional accountancy qualification is not required.

Universities and Colleges

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

The following candidates were successful at the April examination for the Diploma in Obstetrics:

Jessamine M. Akhurst, J. Alexander, H. C. Allen, Anne J. Anderson, M. J. Barnard, C. T. H. Barrett, Renuka Basu, A. G. Blyth, J. G. Blyth, Beryl M. Bromham, J. W. Brown, Jane Buchanan, C. D. Campbell, Margaret E. Chitty, A. R. Chrispin, Elinor B. Clark, Priscilla A. Clark-Maxwell, J. S. Clayton, Elinor M. Cleland, W. M. D. Clements, Mary Clothier, W. G. Cooke, R. L. Coppock, D. C. Cornish, Florence M. Cousley, P. H. Crosskey, Lois R. Davidson, D. W. Davis, D. A. De Renzy-Martin, G. W. Donaldson, D. M. du Toit, C. E. Elliott, Constance H. Ellis, Lucy M. Ellis, E. W. Evans, Joan M. Evans, J. R. Eve, H. T. Fay, Helena M. Fehily, G. Findlay, Kathleen T. Flanagan, J. McC. Forrester, R. W. Galloway, W. F. P. Gammie, R. E. M. Geldart, J. A. Gibson, R. M. Goddard, H. R. Gompertz, J. R. Gough, Sheila M. Gough, J. L. Graham, F. V. Griffiths, A. B. Guest, A. T. G. Gunn, E. A. Haddock, H. N. Hardy, Adeline Kwee-Hong Heah, J. Heffernan, R. M. Hodges, W. S. Hossack, D. S. Iles, Katherine I. Jack, Elizabeth M. Jennings, A. H. John, Isabel D. Johnson, Vivian K. Jones, A. R. Jordan, K. Kelly, A. S. L. Kennedy, Esther S. Kerr, B. Kirsch, W. Lang, L. A. Lees, C. S. Leithead, H. C. Leslie, E. R. Lester, N. H. Logan, P. Los, R. H. Mackay, B. N. McAdam, Kathleen M. McCartie, Doreen E. McConnell, W. E. H. Maeckelberghe, J. M. Manners, Muriel J. Martin, J. F. A. Maskell, H. McI. Morgan, Eleanor Morrison, Mary J. Mossman, K. A. Naylor, Margaret A. Norman, Jean M. North, J. W. Parkin, Rena E. Partridge, W. F. Paveley, J. A. Payne, Mary Phillips, H. R. Playfair, T. A. Plumley, J. G. Powell, Elizabeth M. Price, M. N. Prichard, Margaret J. Purser, Olga M. Rampersaud, Amla Rama Rao, A. M. Reader, D. M. Reader, E. G. Rees, H. F. Reichenfeld, Rosalind M. Rewcastle, D. P. W. Roberts, Margaret J. L. Robinson, R. S. B. Rogers, J. N. Roper, A. D. Rowlands, Hilary M. Rowson, Margaret C. Russell, Dorothy Sanderson, T. A. Sanderson, K. Scott, R. W. Scott, Jane M. Scott-Brown, Jean M. Shields, M. J. Sill, H. R. Simpson, W. S. Sinton, G. H. Smerdon, R. I. Smith, J. H. Spurway, R. M. Stanford, Hilary K. R. Steen, Phyllis A. Stevens, Audrey B. Stevenson, D. Stewart, J. Stewart, T. F. Stoyle, Heather B. Thompson, J. Thompson, D. Tingle, Annemarie D. Tupper, J. Walker, Patricia G. Wallis, W. W. Watson, J. W. S. Webb, J. R. Welsh, B. F. Whiteley, Sheila Wightman, Gladys M. H. Williams, J. R. Wood, W. J. Wright, W. O. C. Young.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **May 28** (No. 21) and corresponding week 1954.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1955					1954				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	10	1	6	0	1	13	0	9	0	0
Dysentery	1,385	55	455	18	2	1,136	142	321	6	2
Encephalitis, acute	2	0		0		6	1	0	0	
Enteric fever:										
Typhoid	1	0	1	2		1	0	0	0	0
Paratyphoid	10	0	2	0		2	0	1	0	0
Food-poisoning	306	16		1		173	20		0	
Infective enteritis or diarrhoea under 2 years				20	10				17	18
Measles*	25,470	923	211	259	301	2,046	42	218	175	314
Meningococcal infection	19	3	16	2		32	0	16	0	0
Ophthalmia neonatorum	64	4	8	0		50	4	9	1	
Pneumonia†	423	19	154	4		428	21	162	5	0
Poliomyelitis, acute:										
Paralytic	12	1	1	1		10	2	3	0	2
Non-paralytic	13	2				6	1			
Puerperal fever§	201	39	7	2		229	29	14	2	
Scarlet fever	609	36	100	49	19	911	60	135	37	51
Tuberculosis:										
Respiratory	744	79	126	21		862	99	213	31	
Non-respiratory	97	7	15	2		128	7	25	7	
Whooping-cough	1,455	71	122	61	35	2,207	81	304	36	27

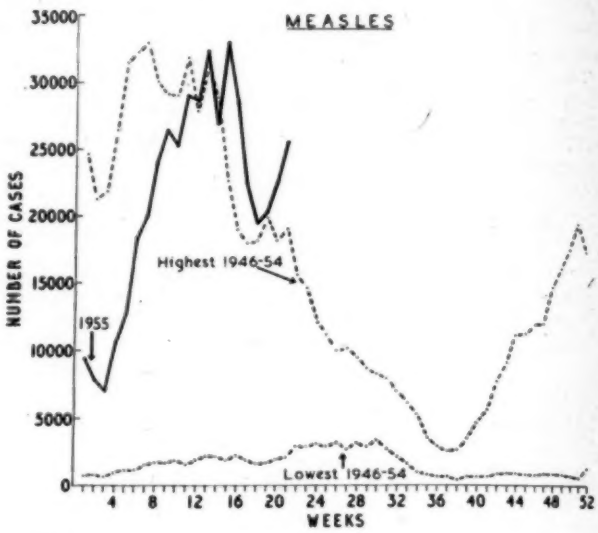
DEATHS in Great Towns	1955					1954				
	Eng. & Wales	Lond.	Scot.	N. Ire	Eire	Eng. & Wales	Lond.	Scot.	N. Ire	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	0	0		0		0	0		0	
Encephalitis, acute		0			0		0	0		0
Enteric fever	1	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	6	0	2	0	1	9	1	2	1	1
Influenza	15	0	0	0	0	5	0	0	1	0
Measles		0	0	0	0		0	0	0	1
Meningococcal infection		0	0				0	1		
Pneumonia	198	21	23	10	8	210	34	20	8	6
Poliomyelitis, acute	1	0			0	0	0	1		0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	72	16	5	4	5	81	11	12	5	7
Non-respiratory		2	2	1	0			2	2	0
Whooping-cough	0	0	0	0	0	0	0	1	0	0
Deaths 0–1 year	219	27	37	5	15	233	24	26	8	9
Deaths (excluding stillbirths)	5,247	716	548	103	173	5,108	679	595	115	185
LIVE BIRTHS	7,838	1103	956	212	440	7,942	1116	901	239	520
STILLBIRTHS	210	35	17			188	17	21		

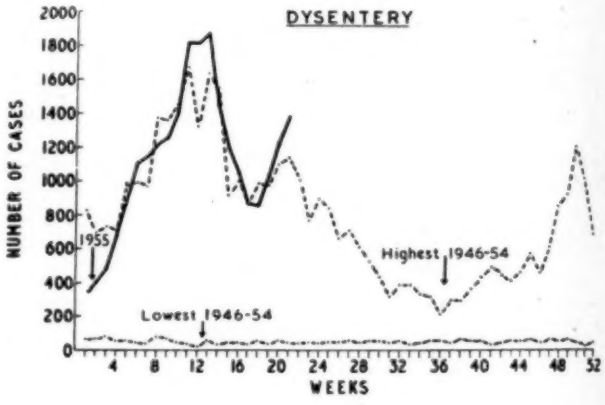
* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

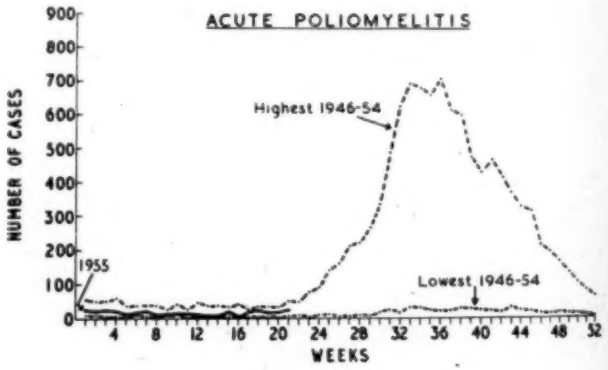
Vital Statistics

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1946–54 are shown thus ------, the figures for 1955 thus ———. Except for the curves showing notifications in 1955, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.







Infectious Diseases

The largest fluctuations in the trends of infectious diseases in England and Wales, during the week ending May 28, were increases of 1,815 for measles, from 23,655 to 25,470, 153 for dysentery, from 1,232 to 1,385, 46 for acute

pneumonia, from 377 to 423, and decreases of 158 for whooping-cough, from 1,613 to 1,455, and 11 for scarlet fever, from 620 to 609. 10 cases of diphtheria were notified, being 7 fewer than in the preceding week.

25 cases of acute poliomyelitis were notified, and these cases were 4 fewer for paralytic and 10 more for non-paralytic cases than in the preceding week. The largest returns were Yorkshire West Riding 5 (Barnsley C.B. 2), Lancashire 4 (Liverpool C.B. 3), and London 3 (St. Pancras 2).

Medical News

Drug Addiction in U.S.A.—The Federal Narcotics Commissioner, Dr. HARRY J. ANSLINGER, testifying before a Senature Judiciary subcommittee in Washington on June 2, gave the number of narcotic addicts in the United States as about 60,000, according to the *New York Times*. This represents an incidence of slightly under 1 in 3,000 of the population, and is based on figures collected since 1953 by the Bureau of Narcotics. New York State accounted for 9,458 of the addicts, and New York itself was stigmatized by the commissioner as "the centre of much of the illicit traffic in heroin." Half the group of "confirmed addicts" were in the age group 21–30 years.

Official Report on the Salk Vaccine.—At 1 a.m. on June 10 the Department of Health Education and Welfare released Dr. L. A. Scheele's report on the Salk vaccine. This followed news that the copy of the report was already in the hands of the *New York Times*. Dr. SCHEELE, Surgeon-General of the U.S. Public Health Service, aided by a committee of experts, has been carrying out a five-week investigation into the reasons for the occurrence of paralytic poliomyelitis in over a hundred of the inoculated children. The report, according to newspaper accounts, makes it clear that inactivation of the three types of virus in the vaccine when undertaken on a commercial scale posed new and difficult problems, and this together with the haste in bringing the product to the public precluded complete safety. The report discloses that on several occasions before Dr. Salk's field trials last year live virus was recovered from some of the batches of vaccine. It seems that the five licensed manufacturing firms had similar troubles, but as such batches were not submitted to the Public Health Service for clearance the authorities were insufficiently aware of the hazard. To deal with this a new Division of Biological Standards has been created and the screening procedure tightened. The report is against the view that the cases of poliomyelitis were due to the injections themselves (post-inoculation poliomyelitis), on the grounds of their geographical distribution. Although no final decision is reached in the report on the question of the banned Cutter vaccine, no good alternative is offered to Professor Gebhardt's explanation that live virus was responsible (see *Journal*, June 11, page 1436). Indeed, in a television interview Dr. Scheele confirmed Professor Gebhardt's claim to have found live virus in one sample of Cutter vaccine.

American Medical Association.—Some 16,000 American doctors, with their wives, attended the 104th annual meeting of the American Medical Association at Atlantic City, New Jersey, from June 6 to 10. Besides the general scientific sessions and the twenty or so specialist sectional meetings, there were colour television programmes of operations and demonstrations from the Hospital of the University of Pennsylvania at Philadelphia, continuous film shows, and a large scientific exhibition. This last had 350 exhibits grouped under scientific sections. A very popular exhibit was the all-day demonstration by six pathologists on fresh post-mortem material; other exhibits were on such things as the chorio-retinal lesions from atomic bomb flash, syphilis in human volunteers, and the electronic analysis of gastro-intestinal sounds. In another part of the exhibition the American Academy of General Practice had cubicles where any doctor could have an immediate chest radiograph and an electrocardiogram. This is expected to become an annual feature. The three principal themes in the scientific sessions were the medical aspects of atomic energy, cardiac surgery, and poliomyelitis.

Nuffield Chair of Child Health at Durham.—Dr. S. D. M. COURT has been appointed to the Nuffield Chair of Child Health at Durham University, left vacant by the death of Sir James Spence a year ago. Dr. Court, who graduated at Birmingham in 1936, has been Reader in Child Health at Durham since 1948. He had previously held appointments at Great Ormond Street and the Westminster Hospital.

Sims Commonwealth Travelling Professors.—The Royal College of Surgeons announces the appointment of Mr. GEOFFREY KEYNES, consulting surgeon to St. Bartholomew's Hospital, and Sir LIONEL WHITBY, Regius Professor of Physic at Cambridge, as Sir Arthur Sims Commonwealth Travelling Professors for 1956. Mr. Keynes will visit Canada and parts of Africa. Sir Lionel Whitby will go to Australia and New Zealand.

Royal College of Surgeons.—At the council meeting on June 9 Mrs. MITCHINER presented the College with two badges of office for the vice-presidents, in memory of her husband, the late Mr. Philip Mitchiner. The Jacksonian Prize was presented to Mr. C. W. D. LEWIS (Cardiff).

Lady Tata Memorial Trust.—In addition to the customary personal grants and scholarships for research on leukaemia and allied diseases, the trustees announce this year a block grant of £1,000 to the Social Medicine Unit at Oxford, directed by Dr. ALICE STEWART, for a pilot inquiry into possible environmental factors in leukaemia.

International Society for Human and Animal Mycology.—This society was founded last year during the eighth International Congress of Botany by a group of scientists from ten nations. The committee is as follows: president, P. REDAELLI (Milan); vice-presidents, C. W. EMMONS (Bethesda), G. T. AINSWORTH (Exeter), P. NEGRONI (Buenos Aires), G. SEGRÉTAIN (Paris); general secretary, R. VANBREUSEGHEM (Antwerp). Those interested in joining the society are invited to write to Dr. R. Vanbreuseghem (Institut de Médecine Tropicale, 155, rue Nationale, Antwerp, Belgium) giving details of their qualifications and a list of their scientific publications.

Care of the Elderly.—The Medical Society for the Care of the Elderly made the following elections to the executive committee at the annual general meeting on May 7: president, Lord AMULREE; hon. vice-presidents, Dr. J. H. SHELDON, Dr. E. L. STURDEE; hon. treasurer, Dr. W. MORTON; hon. secretary, Dr. A. N. EXTON-SMITH; hon. deputy secretary, Dr. P. ARNOLD; other members, Drs. J. AGATE, O. T. BROWN, K. J. G. MILNE, L. NAGLEY, O. OLBRICH, M. WARREN, T. S. WILSON, and Professor R. E. TUNBRIDGE.

Composition of Flour.—Persons or organizations wishing to put evidence before the Government Panel on the Composition and Nutritive Value of Flour are invited to send it in writing before July 9 to the secretary, Miss B. M. Shedden, 10, Whitehall Place, London, S.W.1. Sir HENRY COHEN is chairman of the panel (*Journal*, May 14, p. 1298).

Sweets and Dental Caries.—In the first five years of the Health Service about £100m. was spent on providing artificial teeth. This is stated in a Ministry of Health Circular (11/55) to Local Authorities on the Maternity and Child Welfare Dental Services. In an appendix on the promotion of dental health, the circular blames the greatly increased consumption of sweets as "undoubtedly one of the main causes of the increase in dental decay." The circular quotes in support of this charge the Swedish investigations showing that sugar between meals increases the incidence of caries (see *British Medical Journal*, May 21, p. 1265).

Tour in British West Africa.—There is an opportunity for several United Kingdom medical graduates under the age of 25 on October 31, 1955, to join a small party of young

people visiting British West Africa from November, 1955, to January, 1956. The tour is under the auspices of the Prime Minister's committee on overseas travel parties for youth, which administers moneys allocated from the South African Aid to Britain Fund. Those interested should apply immediately to the tour organizer at 37, Bedford Square, London, W.C.1.

COMING EVENTS

N.A.P.T. Commonwealth Health and Tuberculosis Conference.—The fourth conference will be opened on June 21 at 10 a.m. by the Minister of Health at the Royal Festival Hall, London. After the conference there will be visits to sanatoria, hospitals, and clinics.

Hospitals' Symphony Orchestra.—Concert in the Great Hall of B.M.A. House, Tavistock Square, London, W.C.1, on June 25 at 7.30 p.m. Works by Haydn, Brahms, Dvorak, Sibelius, and Berlioz. Tickets (10s. to 3s. 6d.) from Miss M. A. WHIPP, Almoners' Department, St. Thomas's Hospital, London, S.E.1.

Oxford Graduates' Medical Club.—The Summer Dinner will be held in Oriel College, Oxford, on Friday, July 1, at 7 p.m. with Dr. F. G. HOBSON, D.S.O., F.R.C.P., in the chair. Members may bring medically qualified guests of either sex. Tickets (price 35s.) from RONALD MACBETH, F.R.C.S., Department of Otolaryngology, Radcliffe Infirmary, Oxford.

Irish Medical Association.—Members of the B.M.A. will be welcome at the annual meeting of the I.M.A. at Trinity College, Dublin, July 4–8. Details of the clinical sessions from the secretary of the I.M.A., 10, Fitzwilliam Place, Dublin.

Collegium Internationale Allergologicum.—Symposium on migraine and vascular allergy at Basle, July 3–8.

Royal Medical Benevolent Fund.—Annual general meeting on July 28 at 5 p.m. at 11, Chandos Street, London, W.1.

NEW ISSUES

Journal of Neurology, Neurosurgery and Psychiatry.—The next issue (Vol. 18 (New Series), No. 2) is now available. The contents include:

STUDIES IN TRAUMATIC EPILEPSY, PART 3: VISUAL FITS. W. Ritchie Russell and C. W. M. Whitty.
THE ARTERIAL SUPPLY OF THE SPINAL CORD AND ITS SIGNIFICANCE. D. H. M. Woollam and J. W. Millen.
ENCEPHALITIS IN LOA-LOA FILARIASIS. L. van Bogaert, A. Dubois, P. G. Janssens, J. Radermecker, G. Tverdy, and M. Wanson.
OBSERVATIONS ON THE REACTION TIME TO CUTANEOUS THERMAL STIMULI. P. P. Lele and D. C. Sinclair.
CHRONIC PROLIFERATIVE OSTEITIS OF THE SKULL. J. E. M. Dutton and G. L. Alexander.
THE ASSOCIATION OF DEMENTIA WITH RADIOLOGICALLY DEMONSTRATED CEREBRAL ATROPHY. R. H. Gosling.
CHOROID PLEXUS PAPILLOMA CAUSING SPONTANEOUS SUBARACHNOID HAEMORRHAGE. J. Ernsting.
THE USE OF DEHYDROISOANDROSTERONE IN PSYCHIATRIC PRACTICE. E. B. Strauss and W. A. H. Stevenson.
ISCHAEMIC SENSORY LOSS IN PATIENTS WITH SPINAL AND CEREBRAL LESIONS. R. W. Gilliatt.
ANXIETY AND AN AUTONOMIC REACTION TO PAIN. Malcolm Piercy, Alick Elithorn, R. T. C. Pratt, and Margaret Crosskey.

Issued quarterly; annual subscription £2 2s.; single copy 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

British Journal of Pharmacology and Chemotherapy.—The new issue (Vol. 10, No. 2) is now available. The contents include:

THE ACTION OF HYPNOTIC DRUGS ON FROG SKELETAL MUSCLE. J. P. Quilliam.
THE ACTION OF THIOPENTONE SODIUM ON SKELETAL MUSCLE. J. P. Quilliam.
ACTION OF PROGUANIL AND ITS METABOLITE ON NEUROMUSCULAR AND SYNAPTIC TRANSMISSION. Marcel J. Dallemagne and E. Philippot.
EXPERIMENTAL CHOLERA IN INFANT RABBITS: A METHOD FOR CHEMOTHERAPEUTIC INVESTIGATION. N. K. Dutta and M. K. Habbu.
PROTECTION AGAINST ANAPHYLACTIC SHOCK BY VARIOUS SUBSTANCES. H. Herxheimer.
A POSSIBLE MECHANISM OF ADRENALINE STABILIZATION IN THE ADRENAL GLAND. Douglas G. Humm, Martin Roeder, Miriam Landew, and Eloise E. Clark.
A SERIES OF POLYMETHYLENE BIS-ACETOXYETHYLDIMETHYLAMMONIUM SALTS. R. B. Barlow.
THE ANTICHOLINESTERASE ACTIVITY OF POLYMETHYLENE BIS-QUINOLINIUM SALTS. R. B. Barlow and Jean M. Himms.
THE PHARMACOLOGICAL ACTIONS OF CAPSAICIN AND ANALOGUES. C. C. Toh, T. S. Lee, and A. K. Kiang.
OBSERVATIONS ON HISTAMINE-INDUCED PRURITUS AND PAIN. J. L. Broadbent.
MODIFICATION BY DRUGS OF THE RESPONSE OF THE RAT'S UTERUS TO ADRENALINE. Margarethe Holzbauer and Marthe Vogt.
THE SCHISTOSOMICIDAL ACTIVITY OF SYMMETRICAL DIAMINODIPHENOXYALKANES. C. G. Raison and O. D. Standen.
A SLOW CONTRACTING SUBSTANCE IN NORMAL HUMAN URINE. Fernando P. Gomes.
THE MODE OF ACTION OF SULPHONAMIDES, PROGUANIL, AND PYRIMETHAMINE ON PLASMODIUM GALLINACEUM. I. M. Rollo.
THE RELEASE OF HISTAMINE BY POLYMYXIN B AND POLYMYXIN E. S. R. M. Bushby and A. F. Green.
PHASE-BOUNDARY POTENTIALS AND GANGLION-STIMULANT ACTIVITY. K. A. Exley and P. Hey.
ACTION OF THE HISTAMINE-RELEASER POLYVINYLPYRROLIDONE ON CAPILLARY PERMEABILITY IN DOGS. B. N. Halpern, E. Musso, and Th. Neveu.
BRONCHOCONSTRICTOR AND BRONCHODILATOR ACTIONS OF ANTIHISTAMINE DRUGS. D. F. Hawkins.
A STUDY OF TWO METHODS FOR TESTING LOCAL ANAESTHETICS IN MAN. J. L. Mongar.
PRESENCE OF ACETYLCHOLINE IN THE MALAYAN JACK-FRUIT, ARTOCARPUS INTEGRA. Robert Chun Yu Lin.
RELEASE OF HISTAMINE BY A SUBSTITUTED BUTYLAMINE (L 1935): COMPARISON WITH COMPOUND 48/80. W. Feldberg and J. Lecomte.
STUDIES ON THE MECHANISM OF PITUITARY-ADRENAL ACTIVATION BY MORPHINE. Robert George and E. Leong Way.

Issued quarterly; annual subscription £4 4s.; single copy 25s.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, June 20

BIRMINGHAM MEDICAL INSTITUTE: SECTION OF PSYCHIATRY.—At Central Hospital, near Warwick, 2.30 p.m., clinical meeting.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. Lewis Dexter (Boston): Cor Pulmonale.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., ophthalmology lecture by Dr. D. R. Lucas: Retinal Dystrophy.

Tuesday, June 21

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. O. L. S. Scott: Hypostatic Ulcers.
ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Ernestine Henry Lecture by Dr. K. M. A. Perry: Pulmonary Disease Associated with Metallic Oxides.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—3.45 p.m., Arnott Demonstration by Dr. S. Engel: Post-natal Development of the Child's Lung.
SOUTH-WEST LONDON MEDICAL SOCIETY.—At Bolingbroke Hospital, 8.30 p.m., annual general meeting.

Wednesday, June 22

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Subcutaneous Mycotic Infections.
ROYAL SANITARY INSTITUTE.—2.30 p.m., Mr. P. G. Shute: Role of Mosquitoes in the Spread of Myxomatosis and Some Suggestions for their Control.

Thursday, June 23

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. Haber: The Reticuloses.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. J. C. Gilson: Rheumatism and Lung Disease.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor A. C. Bingold: Benign Fibrous Tumours of Single Bones.
ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., postgraduate demonstration in psychiatry.
●WEST LONDON MEDICO-CHIRURGICAL SOCIETY.—At New Hall, Royal College of Surgeons of England, 7.30 for 8 p.m., annual banquet.

Friday, June 24

CAMBRIDGE MEDICAL SOCIETY.—At Addenbrooke's Hospital, 3 p.m., Mr. S. G. Clayton: Post-maturity.
●INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. P. F. Borrie: Leg Ulcers.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., clinical demonstration by Dr. J. G. Scadding.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—(1) 2 p.m., Mr. J. Bruce: Regional Enteritis. (2) 4 p.m., Mr. P. McG. Moffatt: Use of the Ophthalmoscope in Medicine (II).

Saturday, June 25

CAMBRIDGE UNIVERSITY MEDICAL SCHOOL.—10.30 a.m., symposium: Laboratory Aids to Diagnosis and Treatment.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Clarke-Williams.—On June 8, 1955, at the General Hospital, Rochford, Essex, to Shirley (formerly Hinton), wife of Michael Clarke-Williams, M.B., M.R.C.S., a brother for Marion—Adam Richard.
Dobson.—On June 1, 1955, to Dr. Margaret J. Dobson (formerly Barker), wife of Sydney F. Dobson, Stockport Road, Marple, Cheshire, a second son.

MARRIAGES

Torley—Hausmann.—On December 21, 1954, at The Cathedral, Minden, John Torley, M.B., Ch.B., to Marlies Hausmann, of Minden, Westfalen, Germany.

DEATHS

Gribbell.—On April 13, 1955, at his home, "Torridon," Yelverton, Devon, William Ernest Gribbell, M.R.C.S., L.R.C.P., Surgeon Captain, R.N., retired, aged 78.
Griffiths.—On May 6, 1955, at Ruthin Castle, John Tudor Griffiths, L.R.C.P.&S.Ed., L.R.F.P.S., J.P., of Leaton, Gronant Road, Prestatyn, Flints.
Kilgour.—On April 25, 1955, at 37, Abercon Place, London, N.W., William Robert Kilgour, M.R.C.S., L.R.C.P., aged 71.
Marsh.—On May 4, 1955, at 85, Appleby Lodge, Manchester, Lancs, Frank Needham Marsh, M.B., Ch.B.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Medical Hazards of Travel in France, Spain, and Italy

Q.—*I am planning a motoring tour in France, Spain, and Italy. (a) Is the tap-water safe to drink, and, if not, what precautions are advised? (b) I am told that enteric upsets are particularly common in some parts of France and Spain. Would it be a good idea to take a supply of sulphaguanidine? (c) Am I likely to encounter malaria in these countries, and, if so, what prophylactic measures are advised?*

A.—(*a*) Piped water supplies may generally be regarded as safe throughout France, Spain, and Italy. There is, however, a minimal risk entailed in drinking water from wells or pumps. The risk is so small that most travellers accept it, but it may be eliminated altogether by boiling the water before drinking. This is much more satisfactory than chlorination, which is uncertain and tedious to carry out. If, however, it is desired to chlorinate water, 30 mg. (½ gr.) chloride of lime (calcium hypochlorite) should be dissolved in 1 gallon (4.5 litres); the water is allowed to stand 30 minutes and to it 15 mg. (¼ gr.) sodium thiosulphate (hyposulphite) is then added. The crystals are thoroughly dissolved and the water allowed to stand for a further 30 minutes. The sodium thiosulphate does not play any part in sterilizing the water; it removes excess chlorine and renders it more pleasant to drink.

(*b*) Most enteritic upsets acquired by travellers on the Continent are transient, settling down in a day or two without treatment, but some of them may be cut short by taking standard doses of sulphaguanidine or phthalyl sulphathiazole.

(*c*) The risk of contracting malaria in France, Spain, or Italy is now so small that it may be ignored.

Mild Hookworm Infections

Q.—*If hookworm ova are found in the stools (of a European) is this a definite indication for treatment even though the infestation is light, the blood picture normal, and symptoms absent? What is the prognosis if the case is left untreated?*

A.—No. In such cases the patient will suffer no harm from the presence of the parasites, and they are best ignored. The prognosis is good, though the natural life of the worm may be one of several years. Hookworm infections are difficult to eradicate completely, and to attempt this by repeated courses of treatment is not only usually unsuccessful but also causes anxiety to the patient.

Formalin Fumes

Q.—*A sanitary inspector tells me that the fumes of strong formalin solutions can cause "softening of the brain," and he therefore advises his assistants to handle such solutions only in the open air. Is there any scientific basis for this belief? Are there any other dangers from formalin fumes?*

A.—The vapour of formalin is a powerful upper respiratory irritant, and it is clearly advisable, whenever possible, to prevent a high concentration in a closed space. It is certainly a wise precaution to remove the risk by handling such solutions in the open air. The fluid produces dermatitis of the hands which varies widely in severity. In an appreciable proportion of those who handle fluid formalin an unmistakable degree of hypersensitivity develops, and under these conditions the vapour will aggravate the skin condition. There is no evidence of any association between the inhalation of formalin vapour and "softening of the brain."

Coitus Interruptus and Ejaculatio Praecox

Q.—*What is your expert's opinion of coitus interruptus? A man who has been practising it for several years is now complaining of ejaculatio praecox. What, if any, is the association?*

A.—Coitus interruptus is unsatisfactory because it is an unsafe method of contraception and because, in some couples, it leads to nervous tension and unsatisfied sex urge, with possible psychological and physical reactions. These occur mainly in the wife, but can also present in the husband. Nevertheless it must be admitted that coitus interruptus is the most commonly practised method of contraception, and few of its adherents seem to come to harm.

The suggestion that premature ejaculation in the man in question is a possible psychological reaction to the practice of coitus interruptus over many years is impossible to refute, but it is not very likely. Premature ejaculation is to be regarded as a form of impotence. In early marriage it is often caused by nervousness and inexperience, but after several years of marriage its more probable causes are advancing age with too frequent attempts at coitus, overwork, and the stresses of life in general. Perhaps coitus is attempted with too weak an erection. There may also be hidden factors of a sexual or emotional nature.

Post-mortem Diagnosis of Death from Air Embolism

Q.—*A pathologist found a few air bubbles in superficial cerebral veins at post-mortem examination of a woman who had died suddenly seven hours after colporrhaphy. There was no other abnormality. The coroner accepted his opinion that the death was due to air embolism. Surely it is physiologically impossible for air introduced at the operation site to have reached the cerebral veins.*

A.—It is possible for air to reach the cerebral veins as the result of air embolism in certain cases. This is particularly well seen in abortions due to the use of a Higginson's syringe, when the air is forced into the uterine veins under such pressure that it passes through the right heart and against the stream of blood in the jugular veins to reach the cerebral sinuses and veins. In these cases the sinuses contain very obviously frothy blood, and similar froth will be found in the right heart and jugular veins. The same changes can be found in air embolism due to attempted insufflation of the Fallopian tubes or faulty blood transfusions.

Air may be found in the cerebral veins at post-mortem examination as the result of the tearing of pial and meningeal vessels during the removal of the calvarium. Indeed, it is difficult to avoid the introduction of an occasional bubble of air into these veins, even when considerable care is exercised. For air to persist for seven hours in the cerebral veins between colporrhaphy and death is, in my opinion, impossible. For air to reach the cerebral veins it would have had to be introduced in such volume that it would kill immediately, and its presence would be blatantly obvious in other veins. While air embolism from suicidal cut throat and operations on the neck has occurred as the result of negative pressure in the jugular veins during inspiration, it is difficult to envisage anything like the same mechanism occurring during or after colporrhaphy even in a high Trendelenburg position. The actively contracting pregnant or recently pregnant uterus may trap air and force it into the circulation, but again such conditions do not obtain during colporrhaphy.

To justify a diagnosis of air embolism it should be possible to trace air from a recognized and probable portal of entry, through the veins (in this case the inferior vena cava), to the heart; or to have a clear clinical history of convulsions, transient palsies, haemoptysis, etc., such as are seen in air embolism resulting particularly from artificial pneumothorax procedures. In the absence of air elsewhere in the blood stream, the presence of a few air bubbles in superficial cerebral veins does not justify a diagnosis of air embolism.

Reason for Avoiding Bleeding During Smallpox Vaccination

Q.—*A number of writers describe the technique for smallpox vaccination. All those I have consulted mention that blood should not be drawn in making the scratch. None state the reason. Is it because the blood dilutes the lymph and the vaccination is less likely to "take," or is it more likely that such a scratch will lead to a severe general reaction, with possible generalized vaccinia?*

A.—In the scratch method of vaccination, bleeding is undesirable mainly because blood may wash the virus out of the scratch and also dilute the vaccine, thus reducing its effectiveness. It is unnecessary to scarify deeply, because the "dermal" virus strain employed is adapted to growth in the skin. When the epidermis only is penetrated, as is desirable, a slight oozing of blood-tinged serum may be observed, but little or no blood. The adoption of a technique involving a minimum of trauma may also reduce the risk of post-vaccinal encephalitis and other complications.

The multiple-pressure method of vaccination has now replaced the scratch as the technique of choice in Britain, the United States, and elsewhere. Its advantages include less general "messiness" (with no bleeding) and less risk of septic infection.

Itchy Eruption on a Woman's Shoulders

Q.—*What investigations and treatment are indicated for a healthy woman of 25 whose shoulders are covered with the weals of scratches secondary to lichen simplex or neurodermatitis? The area of spread is over the shoulders and back (latterly improved), and now more marked over waist, hips, and thighs.*

A.—This question does not allow a direct answer. The diagnosis depends as always on the history, including the past history of the patient and that of her family, as well as on the examination. In this way it may be determined whether the condition is a primary eczematous dermatitis or urticaria with secondary eczematization caused by scratching (weals are mentioned). Dermographism may be present. The possibility of lichen planus must be remembered.

If the condition is thought to be eczematous the possibility of allergic sensitization such as occurs with nickel dermatitis from suspender buckles with secondary spread, or rubber dermatitis from a corset or belt, should be considered. On the other hand, the condition may be "constitutional" and related to impairment of general health or to mental stress. The treatment depends on the diagnosis and cannot be discussed here.

Bacterial Flora of the Mouth

Q.—*What is the normal bacterial flora of the mouth and throat? Should one endeavour to eliminate any bacteria found unexpectedly in a routine swab—for example, a staphylococcus?*

A.—The mouth and anterior part of the throat have the most profuse and varied flora of any part of the body with the single exception of the colon, and the inquirer should consult a textbook for a full account of it. Among organisms regularly or frequently found are a great variety of streptococci, *Staphylococcus albus*, strains of *Neisseria*, *Haemophilus* and *Bacteroides*, and spirochaetes (*Treponema dentium*).

Whether an attempt should be made to eliminate any organism found depends: (1) on whether it is potentially pathogenic (a staphylococcus need not be considered further unless it is known to be coagulase-positive); (2) on the likelihood that its presence is connected with anything of which the patient is complaining. A third consideration is the possible risk to other people if a patient is shown to be a carrier of haemolytic streptococci of Lancefield's group A or of virulent diphtheria bacilli.

Kosher Diet and Peptic Ulcer

Q.—*Is there any difference in the incidence of peptic ulceration in those on a strict kosher diet and those who are not?*

A.—There is no direct evidence to suggest that the incidence of peptic ulcer is different in those who take a strict kosher diet and those who do not. Certainly peptic ulcer is common among orthodox Jews.

NOTES AND COMMENTS

Tuberculosis in Pet Monkeys.—Professor E. G. T. LIDDELL, F.R.S. (Oxford), writes: It is well to remember that monkeys in captivity ("Any Questions?" May 14, p. 1232) may be very heavily infected with non-pulmonary tuberculosis and will appear to be in quite good health until a day or two before death. The tuberculin test, even intradermal, is not entirely reliable.

OUR EXPERT replies: What Professor Liddell says is, of course, quite true, but in my reply I said that a negative tuberculin test did not exclude infection and that all pet monkeys should be examined clinically. Such an examination would, of course, include among other things a search for tubercle bacilli in the excreta. Pet guinea-pigs also can suffer from widespread tuberculous infection without showing obvious signs, and, like monkeys, can be a source of infection to their owners. Further, in guinea-pigs the tuberculin test is of little or no value in excluding tuberculosis. Indeed, pet animals of almost any kind are capable of harbouring infections pathogenic to man. I do not, however, consider that this is a valid reason for not keeping pets. Pet-keeping has so many advantages of its own, especially for children, and, provided these risks are realized, the chances of acquiring infection from pets are almost negligible. It is possible to be so obsessed with these risks as to preclude pet-keeping altogether.

Pityriasis Rubra Pilaris.—Dr. DAVID I. WILLIAMS (London, W.1) writes: In the answer to the question on the treatment of pityriasis rubra pilaris ("Any Questions?" May 14, p. 1233) vitamin A in doses of 24,000 units two or three times daily is suggested for treatment. I have found that this dose is often inadequate; a daily total of 480,000 units may be necessary to remove and control the clinical evidence of the disease. I am, of course, aware of the risks, which are not very great, of toxicity with a dose as great as this; but patients prefer to take any risk if their skin condition is completely controlled.

OUR EXPERT replies: The dose mentioned by Dr. Williams is very much higher than is normally considered advisable. It may be that the variable response to vitamin A therapy in this disorder results from inadequate dosage in some cases.

Lack of Beard.—Dr. G. G. SHERRIFF (London, W.8) writes: It was astonishing to read the suggestion of testosterone cream for the healthy man worried by his lack of beard ("Any Questions?" June 4, p. 1399). Surely better advice would have been reassurance and congratulations on his relative freedom from the nuisance of shaving.

Correction.—In the opening paragraph of Dr. M. S. Pathy's medical memorandum on varicella with neurological complications in an adult (May 28, p. 1324), the sentence beginning, "Of the 108 cases with neurological complications . . ." should have been, "Of the 138 cases with neurological complications. . . ."

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